

US008038990B2

(12) **United States Patent**  
**Wang et al.**

(10) **Patent No.:** **US 8,038,990 B2**  
(45) **Date of Patent:** **Oct. 18, 2011**

(54) **COMPOSITIONS AND METHODS FOR THE PREVENTION AND REMOVAL OF BIOFILMS ON INERT AND BIOLOGICAL SURFACES**

2004/0265313 A1 12/2004 Storey et al.  
2005/0053702 A1 3/2005 Elsser  
2005/0059295 A1 3/2005 Chen et al.

(75) Inventors: **Hua Wang**, Columbus, OH (US);  
**Hongliang Luo**, Columbus, OH (US)

(73) Assignee: **The Ohio State University**, Columbus, OH (US)

(\* ) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 610 days.

(21) Appl. No.: **11/421,705**

(22) Filed: **Jun. 1, 2006**

(65) **Prior Publication Data**

US 2007/0059295 A1 Mar. 15, 2007

**Related U.S. Application Data**

(60) Provisional application No. 60/686,629, filed on Jun. 1, 2005.

(51) **Int. Cl.**

**A01N 63/00** (2006.01)  
**A61K 38/46** (2006.01)  
**C12N 9/00** (2006.01)  
**C12N 9/50** (2006.01)  
**C12N 9/52** (2006.01)  
**C12N 1/20** (2006.01)

(52) **U.S. Cl.** ..... **424/93.45**; 424/94.6; 435/183; 435/219; 435/220; 435/252.3; 536/23.2

(58) **Field of Classification Search** ..... None  
See application file for complete search history.

(56) **References Cited**

**U.S. PATENT DOCUMENTS**

5,451,369 A 9/1995 Daeschel et al.  
5,877,272 A 3/1999 Vandenberg et al.  
6,039,984 A 3/2000 Bowling et al.  
6,187,990 B1 2/2001 Runeman et al.  
6,306,391 B1 10/2001 Modi et al.  
6,630,197 B1 10/2003 Wood et al.  
6,692,779 B2 2/2004 Dominiques et al.  
6,703,025 B1 3/2004 Patti et al.  
6,892,732 B2 5/2005 Wang et al.  
6,942,849 B2 9/2005 Neeser et al.  
2002/0012637 A1 1/2002 Neeser et al.  
2002/0025309 A1 2/2002 Modi et al.  
2003/0170184 A1 9/2003 Comelli et al.  
2003/0228297 A1 12/2003 Chang et al.  
2003/0229000 A1 12/2003 Merritt et al.  
2004/0057908 A1 3/2004 Bowen et al.  
2004/0072748 A1 4/2004 Balaban  
2004/0132164 A1 7/2004 Doyle et al.  
2004/0217052 A1 11/2004 Baldrige et al.

**OTHER PUBLICATIONS**

Chica et al. *Curr Opin Biotechnol.* Aug. 2005;16(4):378-84.\*  
Christensson et al. *J Appl Microbiol.* Aug. 2001;91(2):334-43.\*  
Accession Q9AIQ2, Jun. 1, 2001.\*  
Habimana et al. *BMC Microbiol.* May 2, 2007;7:36.\*  
Busscher et al., "Preliminary observations on influence of dairy products on biofilm removal from silicone rubber voice prostheses in vitro", *J. Dairy Sci.* vol. 83, No. 4 (2000), pp. 641-647.  
Busscher et al., "Preliminary observations on influence of dairy products on biofilm removal from silicone rubber voice prostheses in vitro", Exogenous factors influencing voice prosthetic biofilm University of Groningen Dissertation (FREE)(Mar. 2004), Ch. 5, pp. 59-72.  
Free et al., "Biofilm formation on voice prostheses: influence of dairy products in vitro", Exogenous factors influencing voice prosthetic biofilm University of Groningen Dissertation (FREE)(Mar. 2004), Ch. 6, pp. 73-87.  
Klaenhammer et al., "Improved lysis of group *N streptococci* for isolation and rapid characterization of plasmid deoxyribonucleic acid", *Appl. and Environ. Microbiol.*, vol. 35, No. 3 (Mar. 1978), pp. 592-600.  
Luo et al., "High-frequency conjugation system facilitates biofilm formation and pAMBeta1 transmission by *Lactococcus lactis*", *Appl. and Environ. Microbiol.*, vol. 71 (Jun. 2005), pp. 1-9.  
Marsh et al., "A three-tiered approach to differentiate *Listeria monocytogenes* biofilm-forming abilities", *FEMS Microbiology Letters* 11258 (2003), pp. 1-8 (Initial online publication).  
Stentz et al., "Controlled expression of CluA in *Lactococcus lactis* and its role in conjugation", *Microbiology*, vol. 150 (Aug. 2004), (Pt 8), pp. 2503-2512.  
van der Mei et al., "Effect of probiotic bacteria on prevalence of yeasts in oropharyngeal biofilms on silicone rubber voice prostheses in vitro", *J. Med. Microbiol.*, vol. 49, No. 8 (Aug. 2000), pp. 713-718.  
Wang et al., "Analysis of the Physical and functional characteristics of cell clumping in lactose-positive transconjugants of *Lactococcus lactis* ssp. *lactis* ML3", *J. Dairy Sci.*, vol. 77 (1994), pp. 375-384.  
Wang et al., "Interactions between oral bacteria: inhibition of *Streptococcus mutans* bacteriocin production by *Streptococcus gordonii*", *Appl. and Environ. Microbiol.*, pp. 71, No. 1 (Jan. 2005), pp. 354-362.  
Wolz et al., "Transcription of Clumping Factor A in Attached and Unattached *Staphylococcus aureus* in vitro and durin device-related infection", *Infect. Immun.*, vol. 70, No. 6 (Jun. 2002), pp. 2758-2762.

\* cited by examiner

*Primary Examiner* — Christian Fronda

(74) *Attorney, Agent, or Firm* — Calfee, Halter & Griswold LLP

(57) **ABSTRACT**

Organisms, compositions, and methods for at least partially reducing the formation of a biofilm and/or at least partially removing a biofilm are provided. The organisms, compositions, and methods may be used on biotic and abiotic surfaces.

**35 Claims, 11 Drawing Sheets**

1 makanigkll ltgvvsgaia lggsaiyqst tnqsannsrs nttstkvsnv svnvntdvts  
61 aikkvsnsnv svmnyqkdns qssdfssifg gnsgssstd glqlssegsg viykksggda  
121 yvvtnyhvia gnssldvlls ggqkvkasvv gydeytdlav lkissehvkdvatfadsskl  
181 tigepaiavg splgsqfant ategilsats rqvtltqeng qttinaiqt daainpgnsg  
241 galinieggv igitqskitt tedgstsveg lgfaipsndv vniinklead gkisrpalgi  
301 rmvdlsqlst ndssqlklps svtggvvvys vqsglpaasa glkagdvitk vgdtaavtsst  
361 dlqsalyshn indtvkvtyy rdgksntadv klksktsdle tsspsssn

Fig. 1

1 mgrkkkglf llagtvalga lavlpvgeiq akaaisqtk gsslantvta atakqaatdt  
61 taattnqaia tqlaakgidy nklnkvqqd iyvdvqvms aapasengtl rtdysstaei  
121 qgetnkviaa qasvkaaveq vtqqtagesy gyvngfstk vrvvdipklk qiagvktvtl  
181 akvyypdak ansmanvqav wsnkykgeg tvsvidsgi dpthkdmrls ddkdvklts  
241 dvekfddtkv hgryfnskv ygfnyadnd titddkvedq hgmhvagiig angtgddpak  
301 svvgvapeaq llamkvftns dtsattgsdt lvsaiedsak igadvlnmsl gsdsgnqtle  
361 dpeiaavqna nesgtaavis agnsgtsgsa tegvnkdyg lqdnemvgtp gtsrgattva  
421 saentdvitq avtitdgtgl qlgpetiqls sndftgsfdq kkfyvvdas gnlskgkvad  
481 ytadakgia ivkrgeltfd dkqkyaqaag aagliivnd gtatpvtma lttfptfgl  
541 ssvtgqklvd wvtahpddsl gvkiatlv nqkytedkms dftsypvsn lsfkpditap  
601 ggniwstqnn ngytnmsgts maspfiagsq allkqalnknnpfyaykq lkgtaltdfl  
661 ktvemntaqp indinyynvi vsprrqgagl vdvkaaidal eknpstvvaengypavelkd  
721 ftstdktfkl tftnrthel tyqmdsntdt navytsatdp nsgvlydkki dgaakagsn  
781 itvpagktaq ieflslpks fdqqqfvegf lnfkgsdgsr lnlpymgffg dwndgkivds  
841 lngityspag gnfgtvpllt nkntgtqyyg gmvtdadgnq tvddqaiafs sdknalyndi  
901 smkyyllrni snvqvildg qgnkvttlss stnltktyyn ahsqqyiyh apawdgyyd  
961 qrdgniktad dgsytyrisg vpeggdkrqv fdvpfkldsk aptvrhvals aktkngktqy  
1021 yltaevkddl sgldatksvk tainevtnd atftdagtta dgytkietpl sdeqaqalgn  
1081 gdnsaelylt dnasnatdqd asvqkpgsts fdlivngsgl pdkisstttg yeantqgggt  
1141 ytfsgtypaa vdgtytdagg kkhdlnnttyd aatnsftasm pvtnadyaaq vdlyadkaht  
1201 qlkhfdtkv rltaptftdl kfngsdqts eatikvtgtv sadtktvnvg dtvaaldaqh  
1261 hfsvdvpvny gdntikviat dedgnttteq ktitssydpd mlknpvtfdq gvtfgsnefn  
1321 atsakfydpk tgiatitgkv khptttlqvd gkqipikddl tfsftldlgt lgqkpfgvv  
1381 gdttnkftq ealtfildav aptlslsdsst dapvyndpn fqitgtatdn aqylslsing  
1441 ssvasqyadi ninsgkpgm aidqpvkille gknvltvavt dsednttkn itvyepkkt  
1501 laaptvtpst tepaqtvtlt anaatgetv qysadggkty qdvpaagvti tangtfkfs

1561 tdlygnespa vdyvvtnika ddpaqlqaak qaltnliasa ktlsasgkyd datttalaaa  
1621 tqkaqtaldq tnasvdsltg anrdlqtain glaaklpadk ktsllnqlqs vkdalgtldg  
1681 nqtdpstgkt ftaalddlva qaqagtqtdd qlqatlakil devlaklaeg ikaatpaevg  
1741 nakdaatgkt wyadiadtlr sgqasadasd klahlqalqs lktkvaaave adktvgkgdd  
1801 ttgtsdkgsg qgtpapatgd tgkdkgdegs qpssgnipt npatttstst ddttdrngqh  
1861 ttgkgalpkt getterpafg flgvivvilm gvlglkrkqr ee

Fig. 2

1 mkkkmrlkvl lastatalll lsgcqsngtd qtvatysggk vtessfykel kqspttktml  
61 anmliyrain haygksvstk tvndaydsyk qyygenfdaf lsqngfsrss fkeslrtnfl  
121 sevalkkkkk vsesqlkaaw ktyqpkvtvq hiltstedta kqvisdlasg kdfamlaktd  
181 sidtatkdng gkisfelnnk tldatfkdaa yklkngdytq tpvkvtggye vikminhpak  
241 gtftsskkvl tasvyakwsr dssimqrvis qvlknqhvti kdkdladald sykklattn

Fig. 3

1 mkktlrdqll gvskahlnwk nktkvfiygt aillmvapnl assvsrasad eegnapkvtq  
61 agersgklal nishsaldqa isdakaagls lkegaiqdkg naggtadaitk lqkaisddya  
121 sqvstikkqt sdyktalday nkaeadykkq lddiqngidn ntpgspavak gqgltfraqq  
181 npkatvesvk fsgsgdgall kskvlgdgmt glskvtssdv vsqpdfydlg gttslfglfl  
241 dagqsvtity kdlknfslng tsviqmkvty knvtnarmgi mvsrdpgnqf qfgvetngri  
301 fvnqpkalqe slefhdgsnk lmtfktvdss saqfmagsln ysksktpegg lpptsdgynq  
361 hesvsfdntl vvgisyfpssg vkhvsgrpts ganatgdsws snppstnetw satayidyka  
421 igpsldvtew dvgtknswyg amnlipkdqg tsisvtwgtt danmwallng qlpnkiptpe  
481 ppippvkpta tyyydqatfq tdntkavtqt dgtldngalv nkqetenwvl snevlpaghe  
541 viksyvmtdp lpegfkldle qsktlspdyd ltfdektntv tltaykatle amnkdlngay  
601 qvpketlqqg vtkdgssfkn dletlindyt vnsnevevht pdpkpeksne nasgttingq  
661 gidvnatnyy kllwdlsgyk giasskediv rgfyfvdaap dvvdvdlkni sykdsqgkev  
721 kgitakvyss vkdapaevqk vladakiapk gqfvfysvdd pqtftytnyvq tgnnveitqp  
781 mtfkegasga yqntdyqidf gnsyegdtvk nnivppkvvk qvsvdggktw hdskdldpdt  
841 snydykldfn ftangdytki llgdnfessq wtdlakakvt dkdgndiagq fkvlnasgkd  
901 vtkdfnnhvf qkdgkkevlq iiftpdkisd itslasnsdp drlitltmsf kdvtlkgatg  
961 aelanyldke gkivapnigq ldttstrvtg dntkdkitks nvtkvippql tpminkyvye

1021 tgvgsinly dkgltlpsyl sklaqftsln lnkdekvkvg etvhwliatq sgnkslmtnv  
 1081 vdtlplkelsf aenmnakvfv lkndgklgde vtndwkienk gqtltatpnd ptkyffvgss  
 1141 tdsrvvitld ttvneeaktg tftniatint kdggghkedka nvhtkekpet viekitgslp  
 1201 ktgegkaala isifgaallg laaylkrnwi vstyrktvrk irk

Fig. 4

MNKRKEVFGFRKSKVAKTLCGAVLGAALIAIADQQVLADEVTETNSTANVAVTTTGNPATNLPEAQGEATEAASQSQ  
 AQAGSKEGALPVEVSADDLNQA VTDAKAAGVNVVQDQTS DKGTATTAENAQKQAEIKSDYAKQAEI KKTTEAYKK  
 EVEAHQAETDKINAENKAAEDKYQEDLKAHQAEVEKINTANATAKAEYEAKLAQYQKDLAAVQKANEDSOLDYQNKL  
 SAYQAEELARVQKANAEAKEAYEKAVKENTAKNAALQAENEAIKQRNETAKANYDAAMKQYEADLAAIKKAKEDNDAD  
 YQAKLAAYQAEELARVQKANADAKAAYEKAVEENTAKNTAIQAENEAIKQRNAAKATYEAALKQYEADLAAAKKANE  
 DSDADYQAKLAAYQTEELARVQKANADAKAAYEKAVEDNKAKNAALQAENEAIKQRNAAKTDYEAKLAKYEADLAKY  
 KKELAEYPAKPKAYEDEQAQIKAALVELEKNKNQDGYLSKPSAQSLVYDSEPNQSLSLTTNGKMLKASAVDEAFSHD  
 TAQYSKKILQPDNLNVSYLQQADDVTSSMELYGNFGDKAGWTTTVGNNTTEVKFASVLLERQSVTATYTNLEKSYYN  
 GKKISKAVFKYSLSDSKFKNVDKAWLGVLPDPTLGVFASAYTGQEEKDTSIFIKNEFTFYDENDQPINFDNALLSV  
 ASLNRENNSIEMAKDYSGT FVKISGSSVGEKDGKIYATETLNFKQGGSRWMTYKNSQPGSGWDS SDAPNSWYGAG  
 AISMSGPTNHVTVGAISATQVVPSPDPMVA VTKRPNIWYSLNGKIRAVNVPKITKEKPTPPVAPTEPQAPTYEVEK  
 PLEPAPVAPTYENEPTPPVKTPDQPEPSKPEEPTYE TEKPLEPAPVPTYEENEPTPPVKTPDQPEPSKPEEPTYE  
 KPLEPAPVAPTYENEPTPPVKTPDQPEPSKPEEPTYDPLPTPPVAPTPKQLPTPPVVPTVHFHYSSLLAQPQINKEI  
 KNEDGVDIDRTLVAKQSI VKFELKTEALTAGRPKTT SFVLVDPLPTGYKFDLDATKAASTGFDTTYDEASHTVTFKA  
 TDETLATYNADLTKPVETLHPTVVGRVLNDGATYINNFTLTVNDAYGIKSNVVRVTTTPGKPNPDNPNNNYIKPTKV  
 NKNKEGLNIDGKEVLGASTNYEELTWDL DQYKGDKSSKEAIQNGFYVDDY PEEALDVRPDLVKVADEKGNQVSGVS  
 VQQYDSLEAAPKKVQDLLK KANITVKGAFQLFSADNPEEFYKQYVSTGTSLVITDPMTVKSEFGKTGGKYENKAYQI  
 DFGNGYATEVVVNNVPKITPKKDVTVSLDPTS ENLDGQTVQLYQTFNYRLIGGFIPQNHSELEEDYSFVDDYDQAGD  
 QYTGNYKTFSSLNLTMKDGSVIKAGTDLTSQT TAETDAANGIVTVRSKEDSLQKISLDSPFQAETYLQMRRIAIGTF  
 ENTYVNTVNVKAYASNTVVRTTTPIPRTPDKPTPI PTPKPKDPDKPETPKPKVPSPKVEDPSAPIPVSVGKELTTL P  
 KTGTNDSSYMPYLG LAALVGV LGLGQLKRKEDESN

Fig. 5

MKVKKTYGFRKSKISKTLGAVLGTVAAVSVAGQKVFADETTTTSDVDTKVVGTTQGNPATNLPEAQGSASKEAEQS  
 QTKLERQMVHTIEVPKTDLDQAAKDAKSAGVNVVQDADVNGTVKTPPEEAVQKETEIKEDYTKQAEDIKKTDDQYKS  
 DVAAHEAEVAKIKAKNQATKEQYEKDMAAHKAEVERINAANAASKTAYEAKLAQYQADLAQVKTNAANQAAAYQKAL  
 AAYQAEELKRVQEANAAAKAAYDTAVAANNAKNTETIAAANEEIRKRNATAKAEYETKLAQYQAEELKRVQEANAANEAD  
 YQAKLTAYQTELARVQKANADAKATYEAAVAANNAKNAALTAENTAIIKORNENAKATYEAALKQYEADLAQVKKANA  
 ANEADYQAKLTAYQTELARVQKANADAKAAYEAAVAANNAANAALTAENTAIIKRNADAKADYEAKLAKYQADLAKY  
 QKDLADYPVKLKAYEDEQTSIKAALAELEKHKNEEDGNLTPESAQNLVYDLEPNANLSLTTDCKFLKASAVDDAFSFS  
 TSKAKYDQKILQLDDLDITNLEQSNVASSMELYGNFGDKAGWSTTVSNNSQVKWGSVLLERGSATATYTNLQNSY  
 YNGKKISKIVYKYTVDPKSKFQGGQKVLGIFTDPTLGVFASAYTGQVEKNTSIFIKNEFTFYHEDEKPIFNFNALLS  
 VTSLNREHNSIEMAKDYSKGFVKISGSSIGEKNMIYATDTLNFQEGGSRWTMYKNSQAGSGWSSDAPNSWYGA  
 GAIKMSGPNNHVTVGATSATNVMPVSDMPVPGKDNITDGGKPNIIWYSLNGKIRAVNVPKVTKEKPTPPVKPTAPT  
 TYETEKPLKPAPVAPNYEKEPTPPTRTPDQAEPNKPTPPTTYETEKPLEPAPVEPSYEAETPPTRTPDQAEPNKPT  
 PPTTYETEKPLEPAPVEPSYEAETPPPTTPDQPEPNKPVETTYEVIPTPPTDPVYQDLPTPPSDPTVHFHYFKLAVQP  
 QVNKEIRNNNDINIDRTLVAKQSVVKFQLKTADLPAGRDETTSFVLVDPLPSGYQFNPEATKAASPGFDVTDNATN  
 TVTFKATAATLATFNADLTKSVATIYPTVVGQVLNDGATYKNNFTLTVNDAYGIKSNVVRVTTPGKPNPDNPNNNY  
 IKPTKVNKNENGVVIDGKTVLGASTNYEELTWDLQYKNDRSSADTIQKGFYVDDYPEEALELRQDLVKITDANGN  
 EVTGVSVDNYTNLEAAPQEIRDVLSKAGIRPKGAFQIFRADNPREFYDITYVKTGIDLKIVSPMVVKKQMGQTGGSYE  
 NQAYQIDFGNGYASNIVINNVKINPKKDVTLTLDPADTNNVDGQTIPLNTVFNRYRLIGGIIPANHSEELFEYNYD  
 DYDQTDGHTYQYKVFQKVDITLKNVGIKSGTELTQYTTAEVDTTKGAITIKFKEAFLRSVSDSAFQAESYIQMK  
 RIAVGTFFENTYINTVNGVTYSSNTVKTTPEDPADPTDPQDPSSPRTSTVVIYKQSTAYQPSVQETLPNTGVTNN  
 AYMPLLGIIGLVTSFSLGLKAKKD

Fig. 6

MEKGLLDIGRKYWSIAELKRLVLLLQEHKLTHLQLHLNENEGFALNFTDSPVSKKYSENMLKELKEFAKTHEITLI  
 PDFDSPGHMGSLLLEQNPEFALPDSNQQAVDVTNPAVIDWIMGIDKIVDIFPDSDFHIGADEFIDFRQIEKYPYLV  
 EKTREKYGNKASGLEFYDYVNLTEHLQKKGKQVRIWNDGFLRKDLQSLVPLNKNVEVCYWTNWDKGMAEVKEWLT  
 KGYTLINFCNDLYYVLGEEAGYSYPTAEKLEREGKIQKFSGQQYLNQEEMKAVRGTYFSIWADNAAKSVSEILDD  
 LSKVLPVFMKIYGGNDE

Fig. 7

1 mfvkllrsva iglivgail vampslrsln plstpqqfdst detpasynla vrraapavvn  
61 vynrglntns hnqleirtlg sgvimdqrgy iitnkhvind adqiivalqd grvfeallvg  
121 sdsldlavl kinatgg1pt ipinarrvph igdvvlaign pynlgqtitq giisatgrig  
181 lnptgrqnfl qtdasinhgn sggalvnslg elmgintlsf dksndgetpe gigfaipfql  
241 atkimdklir dgrvirgyig iggreiaph aggggidqlg givvnevspd gpaanagiqv  
301 ndliisvdkn paisaletmd qvaeirpgsv ipvvvmrddk qltlqvtiqe ypatn

Fig. 8

MILGNMRGELSMVENQNNNQRPKRNSNAKIITTAIVGVVGGIIGGGVSYAADQMNNATDTTTAQTSVSSNSSKVS  
EKSAKTSGMTTAYNDVKGAVVSVINLKRQSSSSANSLSLFGDDSDSSSGKSGKLETYSEGSSVVMKSNKGY  
IVTNNHVISGSDAVQVQLANGKTVSAKVVGKSTTDLAVLSIDAKYVTQTAEFGDSKSLQAGQTVIAGSPLGSEYA  
STVTQGIISAPARTISTSSGNQQTVIQTDAAINPGNSGGALVNSAGQVIGINSMKLAQSSDGTSVEGMGFAIPSNEV  
VTIVNELVKKGKITRPQLGVRVVALEGIPEAYRSRLKIKSNLKSIGYVASINKNSSAANAGMKSGDVITKVDGKKVD  
DVASLHSILYSHKVGDTVNITINRNGRDVNLKVKLEGN

Fig. 9

MKKFNWKKIVAPIAMLIIGLLGGLLGAFILLTAAGVSFTNTTDTGVKTAKTIVYTNITDFTKAVKKVQNAVVSVINYO  
EGSSSDSLNDLYGRIFGGGDSSDSSQENSKDSGLQVAGEGSGVIYKKGKEAYIVTNNHVVDGAKKLEIMLSDGSK  
ITGELVGKDTYSDLAVVKVSSDKITTVAEFADSNLTVGEKAIAGSPLGTEYANSVTEGIVSSLSRTITMQNDNGE  
TVSTNAIQTDAAINPGNSGGALVNIQVIGINSSKISSTSAVAGSAVEGMGFAIPSNDVVEIINQLEKDGKVT  
LGISIADLNSLSSSATSCLDLPDEVKSGVVVGSVQKGM PADGKLQEYDVITEIDGKKISSKTDIQTNLYSHSIGDTI  
KVTFYRGKDKKTVDLKLTKSTEDISD

Fig. 10

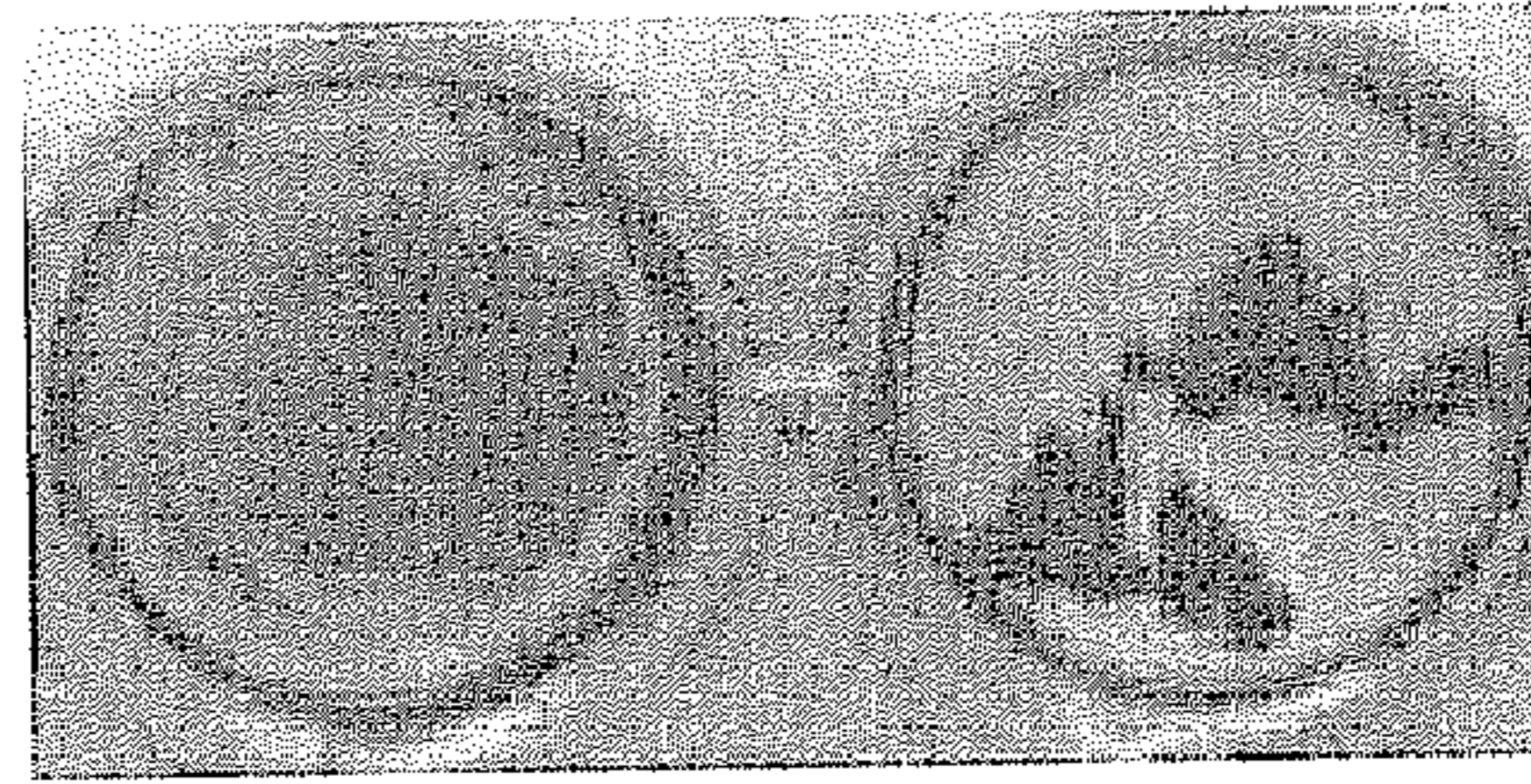


Fig. 11

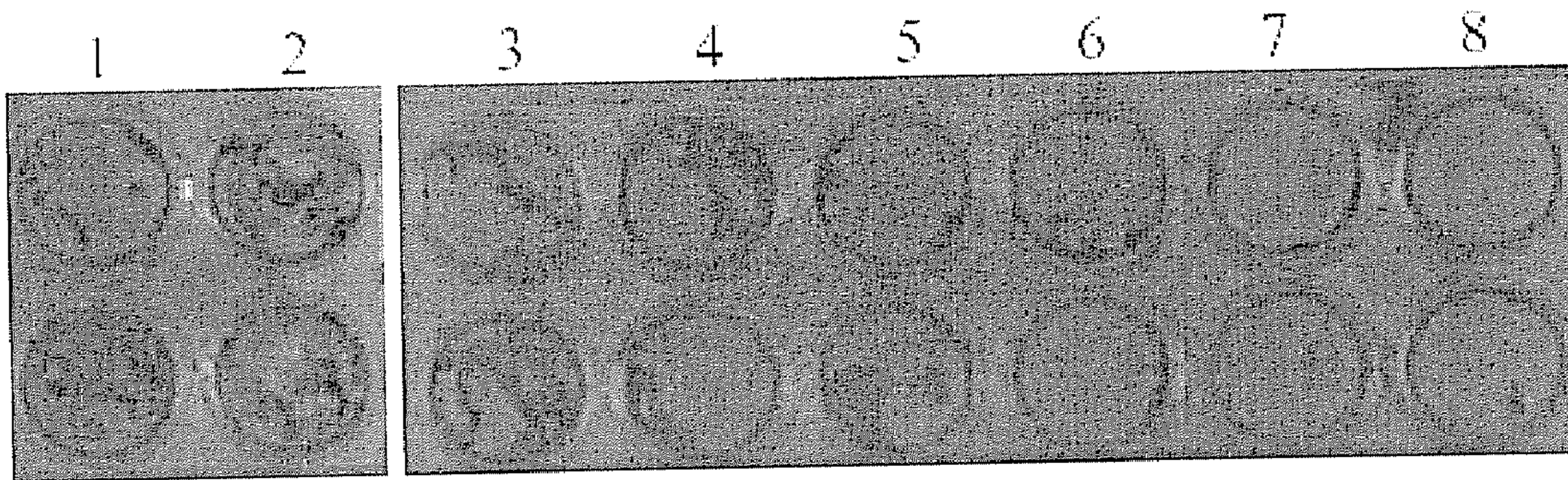


Fig. 12

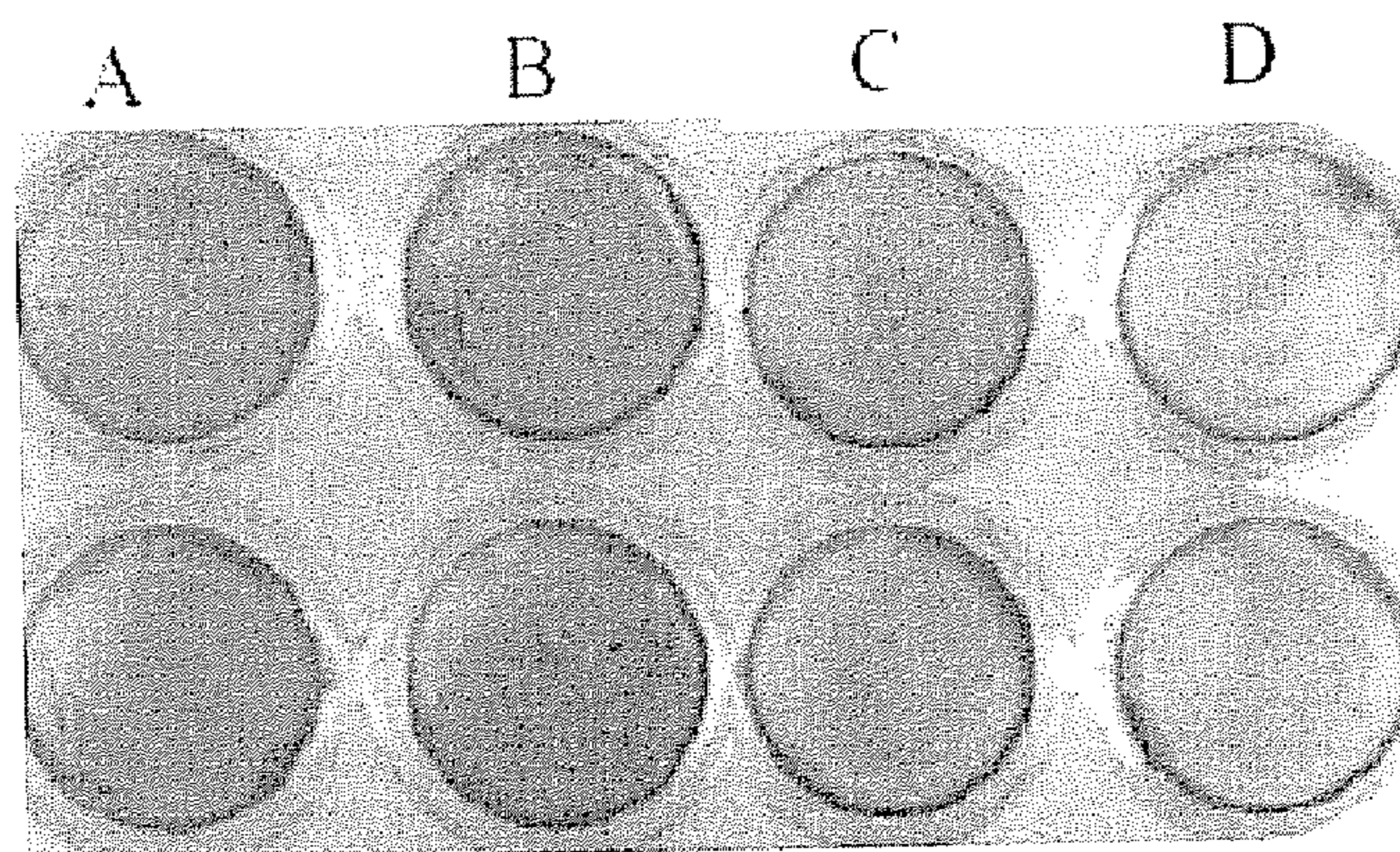


Fig. 13

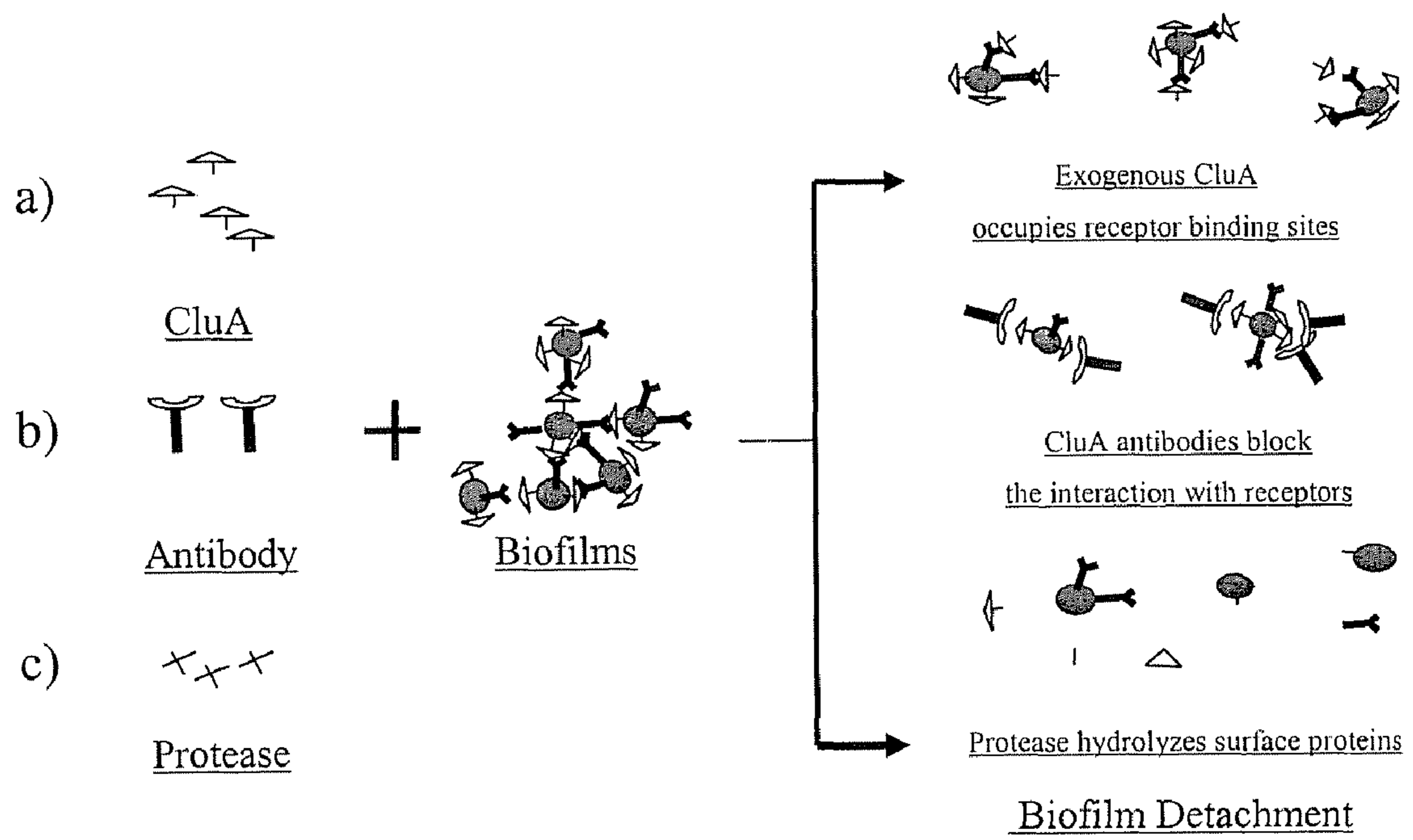


Fig. 14



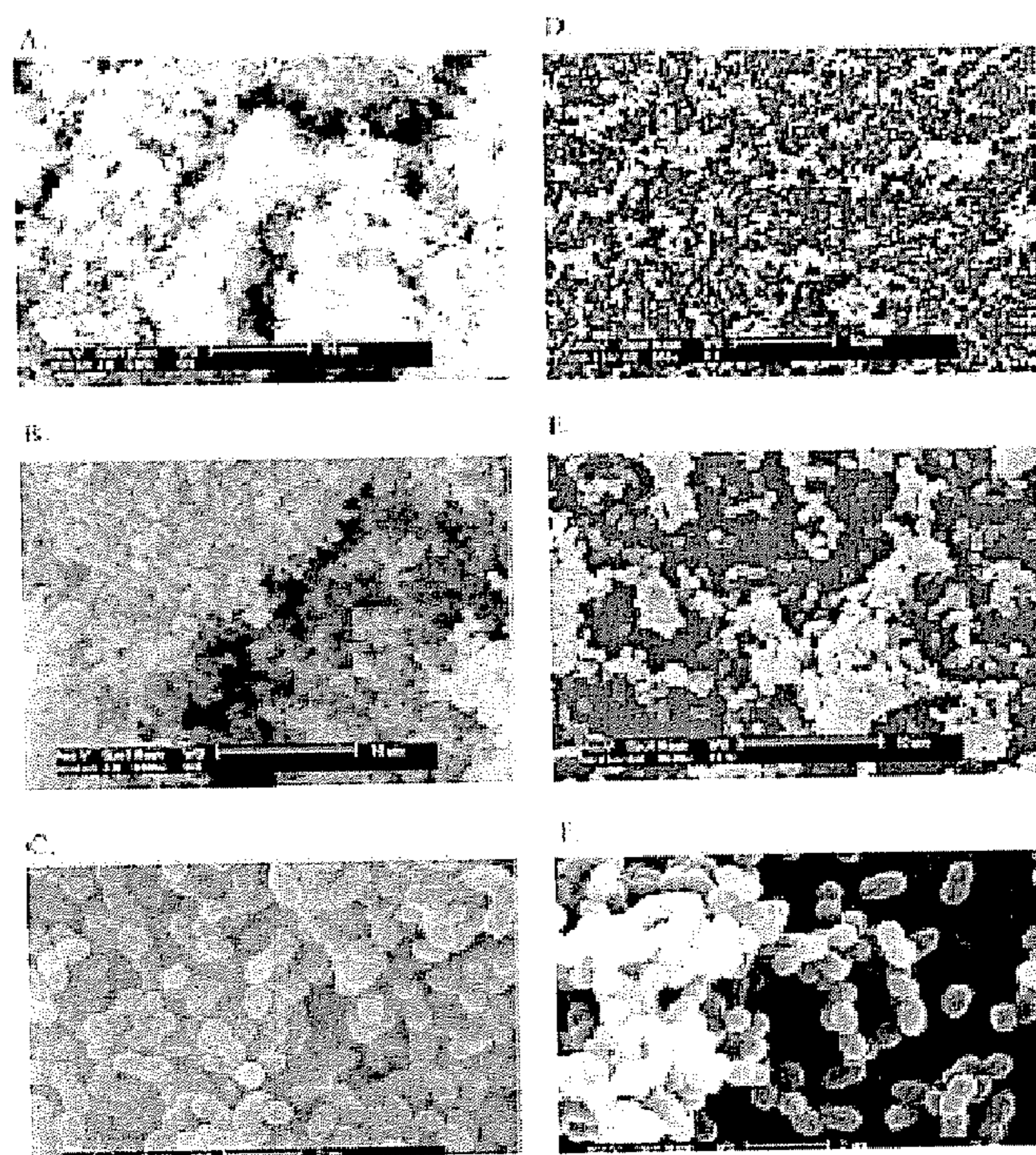


Fig. 15

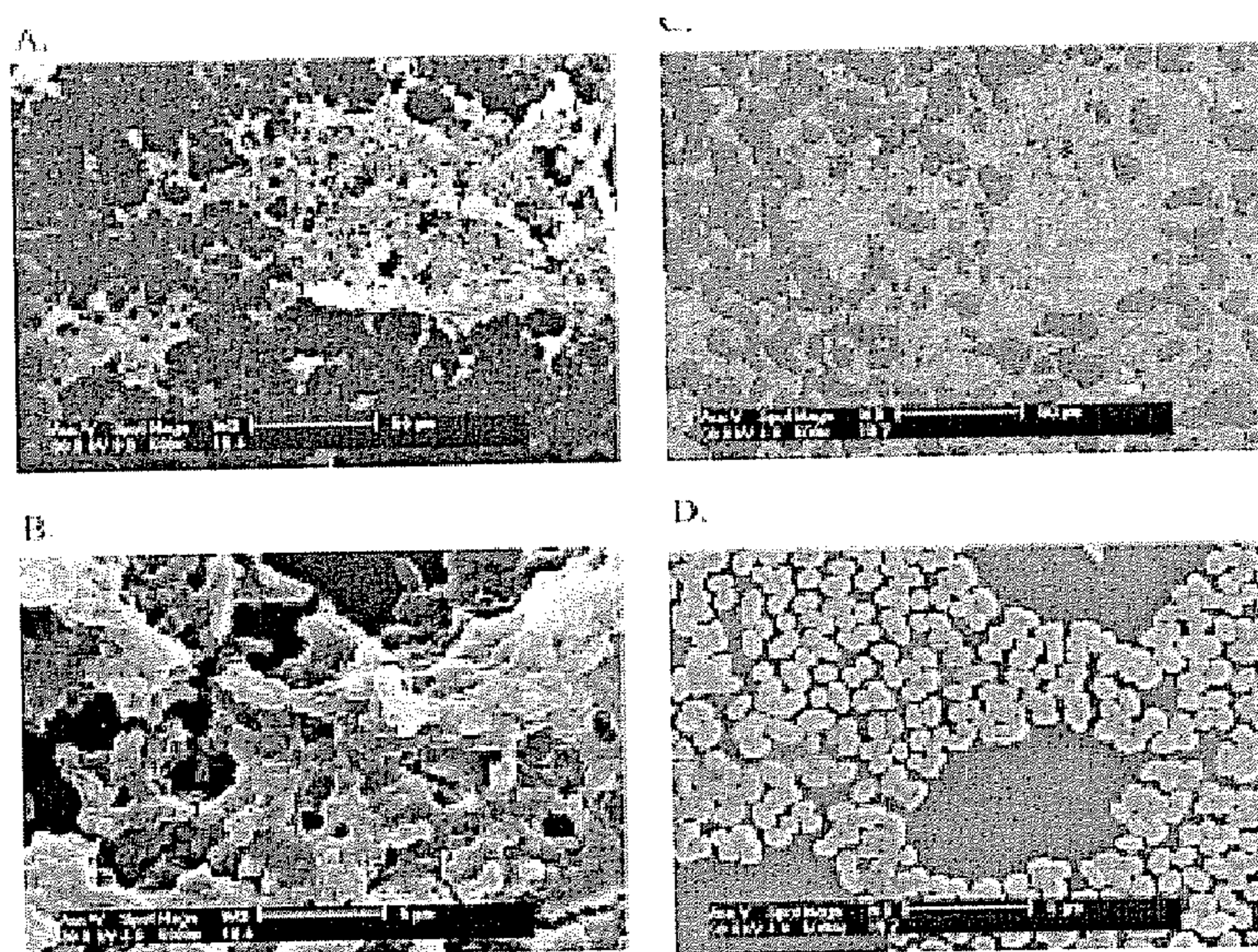


Fig. 16

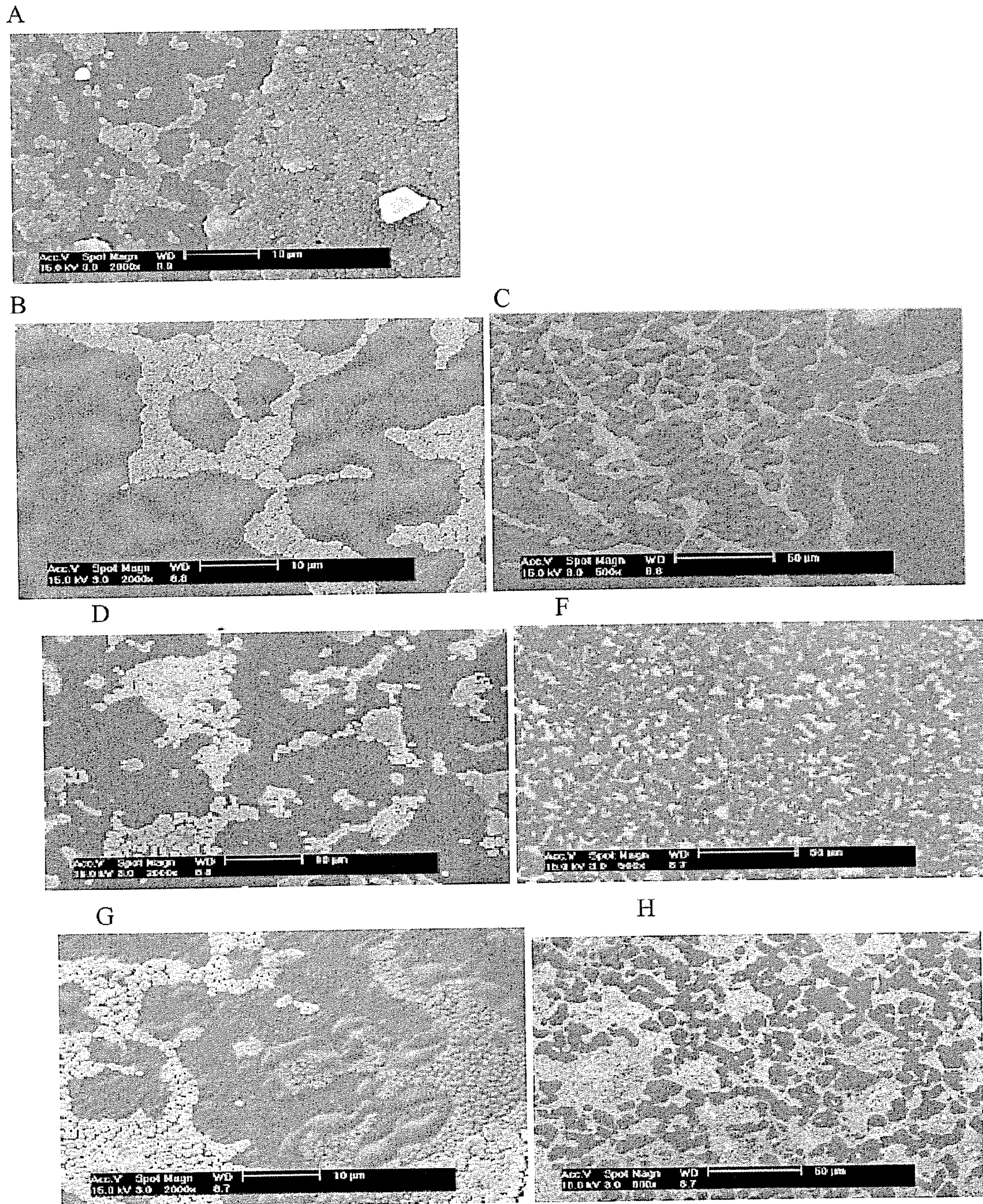


Fig. 17

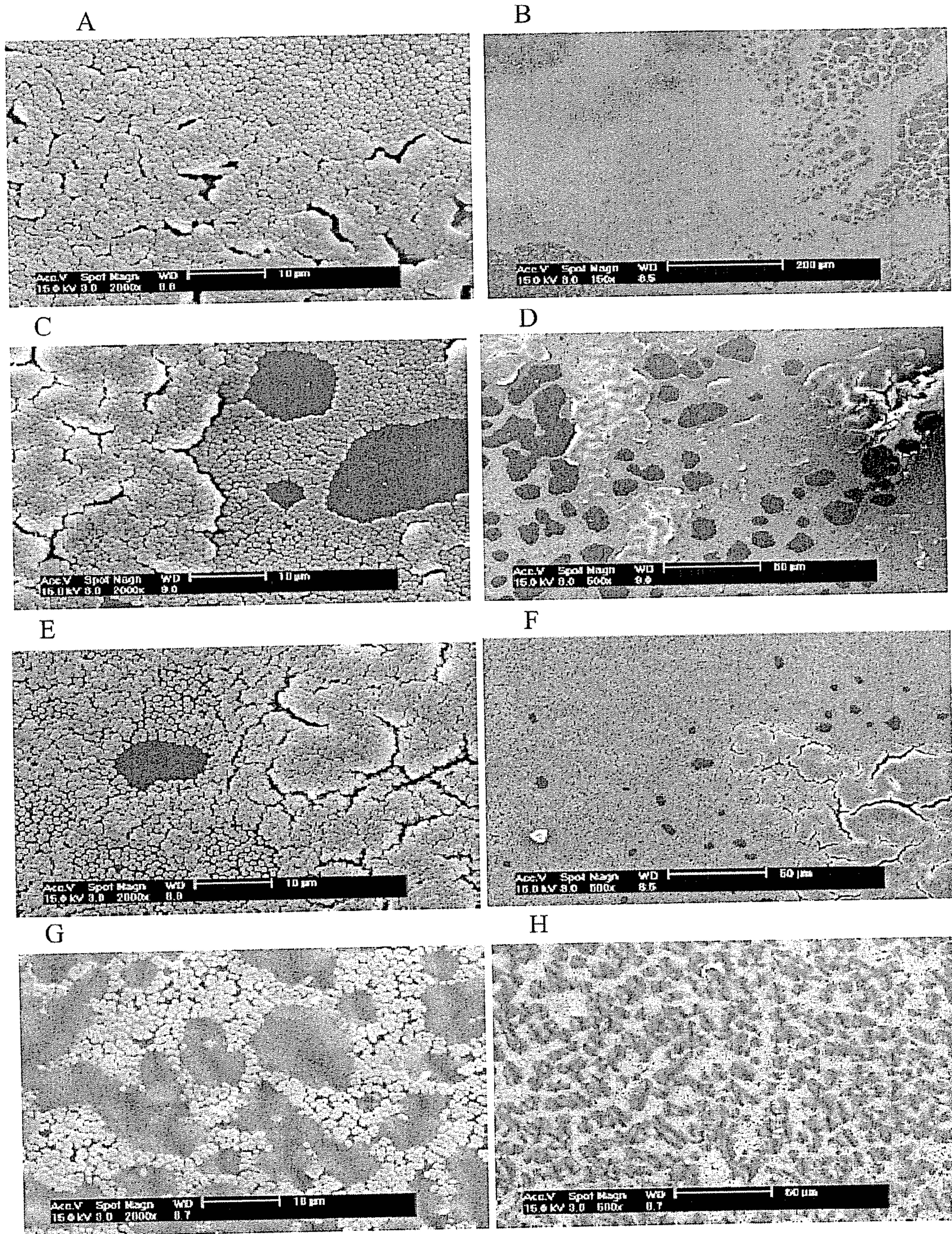


Fig. 18

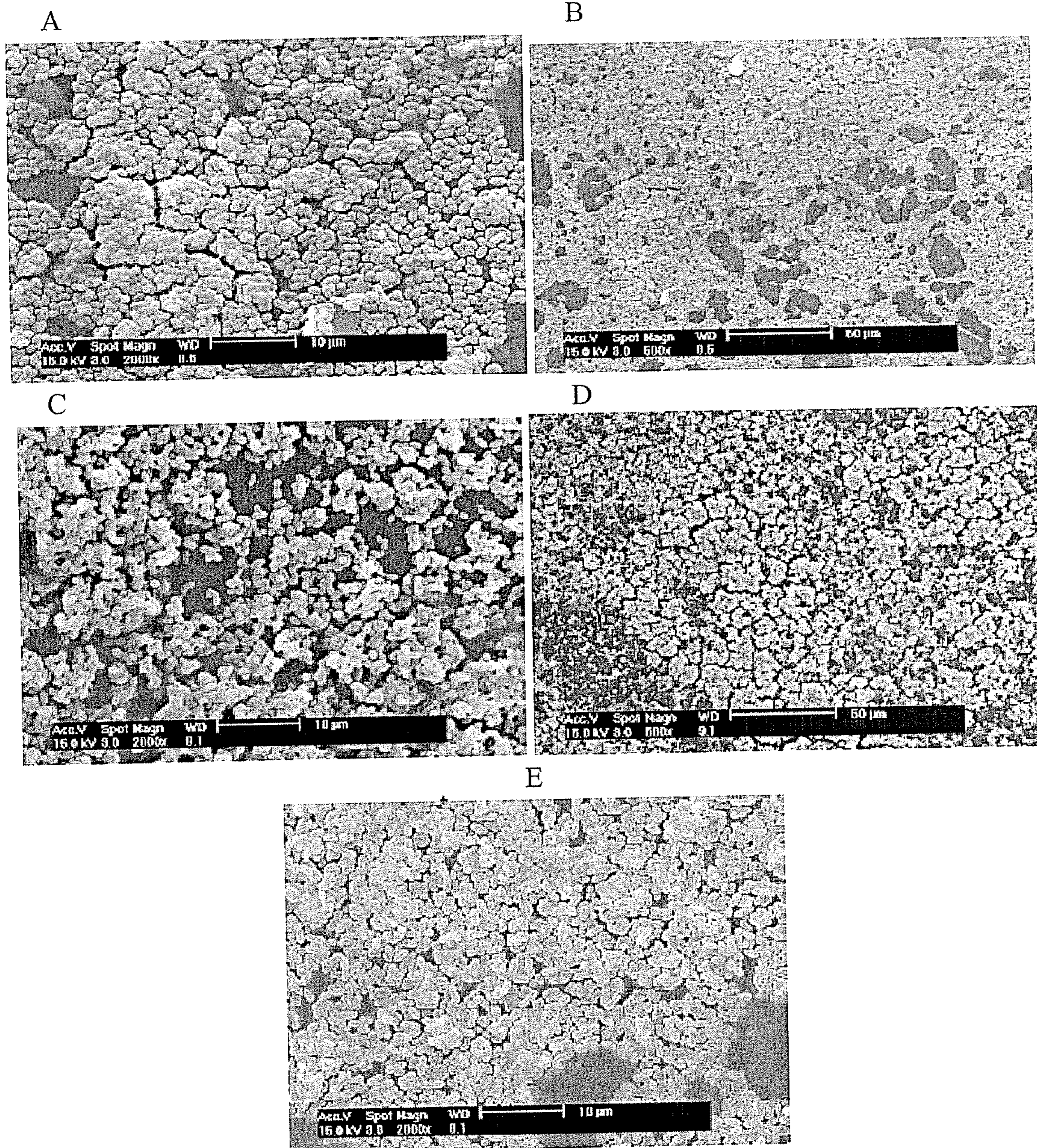


Fig. 19

1

## COMPOSITIONS AND METHODS FOR THE PREVENTION AND REMOVAL OF BIOFILMS ON INERT AND BIOLOGICAL SURFACES

### CROSS REFERENCE TO RELATED APPLICATIONS

This application claims priority to and any other benefit of U.S. Provisional Patent Application No. 60/686,629, filed Jun. 1, 2005, the entirety of which is incorporated by reference herein.

### BACKGROUND

Biofilms are biological films that develop and persist at the surfaces of biotic (biological) or abiotic (inert) objects in aqueous environments from the adsorption of microbial cells onto the solid surfaces. This adsorption can provide a competitive advantage for the microorganisms since they can reproduce, are accessible to a wider variety of nutrients and oxygen conditions, are not washed away, and are less sensitive to antimicrobial agents. The formation of the biofilm is also accompanied by the production of exo-polymeric materials (polysaccharides, polyuronic acids, alginates, glycoproteins, and proteins) which together with the cells form thick layers of differentiated structures separated by water-filled spaces. The resident microorganisms may be individual species of microbial cells or mixed communities of microbial cells, which may include aerobic and anaerobic bacteria, algae, protozoa, and fungi. Thus, the biofilm is a complex assembly of living microorganisms embedded in an organic structure composed of one or more matrix polymers which are secreted by the resident microorganisms.

Biofilms can develop into macroscopic structures several millimeters or centimeters in thickness and cover large surface areas. For non-living objects, these formations can play a role in restricting or entirely blocking flow in plumbing systems, decreasing heat transfer in heat exchangers, or causing pathogenic problems in municipal water supplies, food processing, medical devices (e.g., catheters, orthopedic devices, implants). Moreover, biofilms often decrease the life of materials through corrosive action mediated by the embedded microorganisms. This biological fouling is a serious economic problem in industrial water process systems, pulp and paper production processes, cooling water systems, injection wells for oil recovery, cooling towers, porous media (sand and soil), marine environments, and air conditioning systems, and any closed water recirculation system. Biofilms are also a problem in medical science and industry causing dental plaque, infections (Costerton et al., 1999, *Science* 284: 1318-1322), contaminated endoscopes and contact lenses, prosthetic device colonisation and biofilm formation on medical implants.

Biofilms occur in a wide range of locations. Many are found on or in the human body, including on the teeth, gums, ears, prostate, lungs, and heart, where they are believed to be implicated in chronic infections such as gum disease, ear infections, infections of the prostate gland and heart, and lung infections in people with cystic fibrosis. Biofilms also occur in nature, such as the slime that covers river rocks, marshes, and the like. Biofilms also occur in medical equipment, such as catheters, and are a major source of hospital infections. Biofilms can also occur in areas such as contact lenses; other medical equipment. And biofilms can occur in the food processing and handling industries.

Biofilms produced by oral pathogens are involved in the etiology of some of the most common diseases of the oral

2

cavity, i.e. dental caries, periodontal disease, and peri-implantitis. Formation of oral biofilms is a complex process involving polymicrobial interactions. Neeser et al (US2002/0012637 A1) attempted to treat dental caries, dental plaque and periodontal infections by replacing or limiting pathogenic oral biofilm development with non-residential commensal organisms such as low acidifying lactic acid bacteria that can adhere to the pellicle of the teeth (Neeser et al., US2002/0012637 A1).

Bacteria growing in biofilms are more resistant to antibiotics and disinfectants than planktonic cells and the resistance increases with the age of the biofilm. Bacterial biofilm also exhibits increased physical resistance towards desiccation, extreme temperatures or light. Difficulties in cleaning and disinfection of bacterial biofilm with chemicals is a major concern in many industries. Furthermore, the trend towards milder disinfection and cleaning compositions may increase the insufficient cleaning of surfaces covered with biofilm.

Accordingly, there exists a need for improved methods and new systems and compositions that can reduce or eliminate biofilms and/or the formation of biofilms on inert and biological surfaces.

### SUMMARY OF THE INVENTION

In accordance with embodiments of the present invention, methods for preventing or removing a biofilm are provided. The methods can comprise contacting a biofilm or a biofilm surface with a composition such that biofilm formation on the biofilm surface is reduced or the biofilm is at least partially removed. The composition can comprise at least one of an organism that overexpresses one or more of *Lactococcus lactis* HtrA, *Lactococcus lactis* PrtP, *Lactococcus lactis* PrtM, *Lactococcus lactis* CluA, *Streptococcus gordonii* SspA, *Streptococcus mutans* Pac, *Lactococcus lactis* InbA, *Lactobacillus johnsonii* HtrH-like proteinase, *Lactobacillus acidophilus* HtrH-like proteinase, and *Streptococcus thermophilus* exported proteinase, isolated *Lactococcus lactis* HtrA, isolated *Lactococcus lactis* PrtP, isolated *Lactococcus lactis* PrtM, isolated *Lactococcus lactis* CluA, isolated *Streptococcus gordonii* SspA, isolated *Streptococcus mutans* Pac, isolated *Lactococcus lactis* InbA, isolated *Lactobacillus johnsonii* HtrH-like proteinase, isolated *Lactobacillus acidophilus* HtrH-like proteinase, and isolated *Streptococcus thermophilus* exported proteinase.

It will be understood both the forgoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the invention as claimed.

### BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS

The following detailed description of embodiments of the present invention can be best understood when read in conjunction with the following drawings, where like structure is indicated with like reference numerals and in which:

FIG. 1 illustrates the *Lactococcus lactis* HtrA sequence (SEQ ID NO: 1);

FIG. 2 illustrates the *Lactococcus lactis* Proteinase (PrtP) sequence (SEQ ID NO: 2);

FIG. 3 illustrates the *Lactococcus lactis* PrtM sequence (SEQ ID NO: 3);

FIG. 4 illustrates the *Lactococcus lactis* CluA sequence (SEQ ID NO: 4);

FIG. 5 illustrates the *Streptococcus gordonii* cell surface protein (SspA) sequence which has homology to CluA (SEQ ID NO: 5);

FIG. 6 illustrates the *Streptococcus mutans* Pac protein sequence which has homology to CluA (SEQ ID NO: 6);

FIG. 7 illustrates the *Lactococcus lactis* InbA sequence (SEQ ID NO: 7);

FIG. 8 illustrates the *Lactobacillus johnsonii* HtrH like proteinase (SEQ ID NO: 8);

FIG. 9 illustrates the *Lactobacillus acidophilus* HtrH like proteinase (SEQ ID NO: 9);

FIG. 10 illustrates the *Streptococcus thermophilus* exported proteinase (SEQ ID NO: 10);

FIG. 11 shows attached versus detached biofilms, left: LM2301 and right: HW002;

FIG. 12 shows *L. lactis* HW002 Bfm with (1) 10 mM PMSF, (2) 5 mM PMSF, (3) 1 mM PMSF, (4) no addition, (5) 200 µg proteinase, (6) 400 µg proteinase, (7) 1 proteinase, (8) 2 mg proteinase;

FIG. 13 shows detachment of 48 h staphylococcal biofilms by lactococci. A, *Staphylococcus* spp. HLZ biofilm (no treatment); B, *Staph* biofilm+*Pseud.* spp. HLY, 2 h 30° C. (control); C, *Staph* biofilm+*L. lactis* LM2301, 2 h 30° C.; D, *Staph* biofilm+*L. lactis* HW002, 2 h 30° C.;

FIG. 14 illustrate strategies for biofilm detachment;

FIG. 15 show SEM pictures of biofilm formation by *L. lactis* HL3A. A: With nisin induction. D: Without nisin induction. B, C and E, F: Regional magnification of A and C;

FIG. 16 shows SEM pictures of biofilm formation by *L. lactis* HL2301A. A and B: With nisin induction. C and D: Without nisin induction;

FIG. 17 shows SEM pictures of biofilm formation of *Lactococcus lactis* LM2302: FIG. 18A is the control; FIGS. 18B-C are with casein; FIGS. 18D-E are with proteinase; and FIGS. 18F-G are with PMSF

FIG. 18 shows SEM pictures of biofilm formation of SK11-1, a plasmid cured derivative of SK11: FIGS. 19A-B are the control; FIGS. 19C-D are with casein; FIGS. 19E-F are with PMSF.; and FIGS. 19G-H are with proteinase;

FIG. 19 shows SEM pictures of biofilm formation of SK11, a parental strain that carries multiple plasmids including those encoding for proteinases PrtP and PrtM: FIG. 20A-B are the control; FIGS. 20C-D are with casein; FIGS. 20E-F are with PMSF; and FIG. 20G is with proteinase.

#### DETAILED DESCRIPTION OF EMBODIMENTS OF THE INVENTION

The present invention will now be described with occasional reference to the specific embodiments of the invention. This invention may, however, be embodied in different forms and should not be construed as limited to the embodiments set forth herein. Rather, these embodiments are provided so that this disclosure will be thorough and complete, and will fully convey the scope of the invention to those skilled in the art.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. The terminology used in the description of the invention herein is for describing particular embodiments only and is not intended to be limiting of the invention. As used in the description of the invention and the appended claims, the singular forms "a," "an," and "the" are intended to include the plural forms as well, unless the context clearly indicates otherwise. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety.

This invention is based on the unexpected discovery that one or more bacterial proteins and/or proteinases from lactic acid bacteria and other bacteria and homologs of these proteins and proteinases, for example the lactic acid bacteria *Lactococcus lactis*, function to prevent or diminish the association between bacteria in biofilms, thus presenting the possibility for use of the bacteria, or one or more of the bacterial proteins and/or proteinases, alone or combined, to reduce the formation of and/or at least partially remove biofilms.

In accordance with embodiments of the present invention, bioengineered bacterial organisms are provided. The bioengineered bacterial organisms are bioengineered to express two or more of the bacterial proteins and/or proteinases of interest. The bacterial proteins and/or proteinases of interest may be any suitable bacterial protein or proteinase that interact with surface molecules on target bacterial cells, such as pathogenic bacteria, or otherwise undesirable bacteria, to prevent surface attachment of the cells and interaction between the cells. Suitable proteins and proteinases include, but are not limited to: *Lactococcus lactis* HtrA SEQ ID No: 1 (FIG. 1), *Lactococcus lactis* PrtP SEQ ID No: 2 (FIG. 2), *Lactococcus lactis* PrtM SEQ ID No: 3 (FIG. 3), *Lactococcus lactis* CluA SEQ ID No: 4 (FIG. 4), *Streptococcus gordonii* SspA SEQ ID No: 5 (FIG. 5), *Streptococcus mutans* Pac SEQ ID No: 6 (FIG. 6), *Lactococcus lactis* InbA SEQ ID No: 7 (FIG. 7), *Lactobacillus johnsonii* HtrH-like proteinase SEQ ID No: 8 (FIG. 8), *Lactobacillus acidophilus* HtrH-like proteinase SEQ ID No: 9 (FIG. 9), and *Streptococcus thermophilus* exported proteinase SEQ ID No: 10 (FIG. 10). It will be understood that suitable variants of SEQ ID Nos:1-10 may also be used. Additionally, suitable homologs may be used. These proteins and proteinases will be discussed further herein. Bioengineered bacterial organisms can promote the inhibition or removal of a biofilm. It will be understood that these bacteria can be constituted in formulations as are well known in the art for achieving shelf-stability, and may be provided in the form of non-ingestible or ingestible products for use in treating inert or biological surfaces.

It will be understood that the bioengineered bacterial organisms can be formed in any suitable manner. For example, the bioengineered bacteria can comprise variant forms of *Lactococcus lactis*, other lactic acid bacteria, or other bacteria as further described herein, or combinations of these. In other examples, the bacteria can comprise other non-pathogenic bacteria containing polynucleotide vectors which include appropriate promoters in operable communication with one or a combination of polynucleotides encoding one or more of the proteins or proteinases of interest. It will be further understood that the bioengineered organisms can be provided in any suitable manner, including, but not limited to in suspension, immobilized on an abiotic matrix, in a gum, or in a cheesy tooth paste.

In accordance with additional embodiments of the present invention, compositions that at least partially inhibit or at least partially remove a biofilm are provided. The compositions comprise an effective amount of two or more proteins or proteinases and/or bacteria that overexpress at least one of the proteins or proteinases of interest. For example compositions that comprise an effective amount of two or more of isolated *Lactococcus lactis* HtrA, *Lactococcus lactis* PrtP, *Lactococcus lactis* PrtM, *Lactococcus lactis* CluA, *Streptococcus gordonii* SspA, *Streptococcus mutans* Pac, *Lactococcus lactis* InbA, *Lactobacillus johnsonii* HtrH-like proteinase, *Lactobacillus acidophilus* HtrH-like proteinase, and *Streptococcus thermophilus* exported proteinase and/or bacteria overexpressing one or more of *Lactococcus lactis* HtrA, *Lactococcus lactis* PrtP, *Lactococcus lactis* PrtM, *Lactococcus lactis*

CluA, *Streptococcus gordonii* SspA, *Streptococcus mutans* Pac, *Lactococcus lactis* InbA, *Lactobacillus johnsonii* HtrH-like proteinase, *Lactobacillus acidophilus* HtrH-like proteinase, and *Streptococcus thermophilus* exported proteinase.

It will be understood that the bacteria can be any suitable bacteria. For example, the bacteria may be wild-type or variant forms of *Lactococcus lactis*, other lactic acid bacteria, or other bacteria as further described herein, or combinations of these. In some embodiments, the bacteria comprise other non-pathogenic bacteria containing polynucleotide vectors which include appropriate promoters in operable communication with one or a combination of polynucleotides encoding one or more of the proteins and/or proteinases of interest.

In yet other embodiments, the invention provides compositions for at least partially preventing or removing biofilms. The compositions one or more antibodies directed to one or more of *Lactococcus lactis* CluA, *Streptococcus gordonii* SspA, and *Streptococcus mutans* Pac or the receptors therefore. Additionally, the compositions can further comprise one or more of *Lactococcus lactis* HtrA, *Lactococcus lactis* PrtP, *Lactococcus lactis* PrtM, *Lactococcus lactis* CluA, *Streptococcus gordonii* SspA, *Streptococcus mutans* Pac, *Lactococcus lactis* InbA, *Lactobacillus johnsonii* HtrH-like proteinase, *Lactobacillus acidophilus* HtrH-like proteinase, and *Streptococcus thermophilus* exported proteinase.

The compositions can comprise any suitable additives and/or additional active ingredients. For example, the compositions can further include surfactants, therapeutics, and/or antimicrobials. In other embodiments, the compositions may further comprise other additives such as colorants, stabilizers, flavorings for use in treatment or prevention of biofilms in the oral cavity. In yet other such embodiments, the compositions may further comprise other additives such as colorants, stabilizers, antimicrobials, perfumes, and the like for use in treatment or prevention of biofilms in industrial or residential settings. In still yet other such embodiments, the compositions may further comprise other additives suitable for use in treatment or prevention of biofilms in the healthcare delivery or medical device handling settings. It will be understood that the compositions can be provided in any suitable manner, including, but not limited to in suspension, immobilized on an abiotic matrix, in a gum, or in a cheesy tooth paste.

In accordance with yet further embodiments, the compositions and/or bioengineered bacteria may be used to reduce the formation of biofilm on a surface and/or at least partially remove a biofilm. For example, methods for preventing or removing a biofilm can comprise contacting a biofilm or a biofilm surface with a composition comprising at least one of an organism that overexpresses one or more of *Lactococcus lactis* HtrA, *Lactococcus lactis* PrtP, *Lactococcus lactis* PrtM, *Lactococcus lactis* CluA, *Streptococcus gordonii* SspA, *Streptococcus mutans* Pac, *Lactococcus lactis* InbA, *Lactobacillus johnsonii* HtrH-like proteinase, *Lactobacillus acidophilus* HtrH-like proteinase, and *Streptococcus thermophilus* exported proteinase, isolated *Lactococcus lactis* HtrA, isolated *Lactococcus lactis* PrtP, isolated *Lactococcus lactis* PrtM, isolated *Lactococcus lactis* CluA, isolated *Streptococcus gordonii* SspA, isolated *Streptococcus mutans* Pac, isolated *Lactococcus lactis* InbA, isolated *Lactobacillus johnsonii* HtrH-like proteinase, isolated *Lactobacillus acidophilus* HtrH-like proteinase, and isolated *Streptococcus thermophilus* exported proteinase such that biofilm formation on the biofilm surface is reduced or the biofilm is at least partially removed.

In other embodiments, the composition can also include one or more antibodies to one or more of *Lactococcus lactis* CluA, *Streptococcus gordonii* SspA, and *Streptococcus*

*mutans* Pac or the receptors therefore. In yet further embodiments, the composition can comprise one or more such antibodies.

The methods may be used to contact any suitable surface and/or biofilm. For example, the step of contacting can comprise contacting an oral surface and/or a biofilm on an oral surface or an abiotic surface and/or a biofilm on an abiotic surface. Additional biotic surfaces and/or biofilms on biotic surfaces can be contacted. The contact can occur in any suitable manner for any length of time. For example, the composition can contact the biofilm for a period of time such that the biofilm is at least partially removed. In another example, the composition can contact the biofilm surface for a period of time such that biofilm formation on the biofilm surface is reduced.

In certain embodiments, the compositions comprising bacteria expressing one or more of CluA, PrtP and HtrA are used to prevent or treat biofilms of the oral cavity. In other embodiments, the compositions are used to treat inert, abiotic surfaces, such as equipment, tables, instruments, storage and mixing vessels, and the like, used in a variety of industries, including healthcare, medical devices, food preparation and storage, and others. More generally, in the various embodiments described herein the methods and compositions are suitable for treating or preventing biofilms on a wide variety of surfaces and in a wide range of contexts.

Having discussed particular embodiments of the invention herein, particular proteins and proteinases of interest, along with particular modes of action, will now be discussed. Although the bacteria *L. lactis* are abundant in fermented foods (such as cheese) as fermentation starter cultures, they are rarely found as residential organisms in the oral ecosystem. A model organism *L. lactis* HW002 is a clumping transconjugant derived from mating the donor strain ML3 and the recipient LM2301. Comparing to the donor strain ML3, this strain has overexpressed CluA protein, which is believed to be a key biofilm attribute. Besides CluA, a second plasmid encoded element is involved in *L. lactis* biofilm from initiation to detachment.

FIG. 11 shows that LM2301 formed a light biofilm, but the transconjugant HW002 (LM2301 received the Lac plasmid and the sex factor) not only exhibited facilitated biofilm formation (thicker) but detachment as well. Another key component encoded by the Lac plasmid is the proteinase PrtP. The cloned and sequenced HW002 prtP gene has high homology with published proteinases from all lactic acid bacteria such as *Lactobacillus casei*, *Streptococcus thermophilus*, *Lb. acidophilus* etc, as well as streptococcal proteinases, including those from oral streptococci (Appendix A).

HW002 exhibited facilitated biofilm formation as well as detachment phenotype. CluA is highly homologous to key oral streptococcal surface adhesins involved in biofilm formation. FIG. 12 shows that exogenous proteinase treatment can simulate the function of PrtP and facilitate biofilm removal. Adding proteinase inhibitor has the opposite effect. Protease treatment affecting the functionality of the key cell surface proteins such as CluA facilitated biofilm detachment. The lactococcal surface proteases such as PrtP and HtrA are the matching endogenous molecules that are responsible for degradation of the lactococcal proteins including those involved in biofilm formation. Other lactic acid bacteria such as *lactobacilli* also carry the proteinases but are able to integrate into oral ecosystem. The major difference is lactococcal PrtP is encoded by the plasmid therefore the dose of expression is much higher than other lactic acid bacteria (LAB) as well as streptococci, where the prtP gene is chromosomal located (single copy). Genome sequence search indicated that

several LAB strains such as *Lb. casei* and *Lb. helveticus* carry multiple copies of surface proteinases in the chromosome, therefore these LAB strains will have facilitated biofilm detachment as well.

Environmental stress that can trigger Htr proteinases expression will also facilitate biofilm detachment. HW002 carrying the active ingredients are also functional in breaking biofilms by other organisms besides lactococci (FIG. 13). The overwhelming activities of proteinase activities (both plasmid and chromosomal located) are components in biofilm detachment and are believed to be responsible for the observed lacking of lactococci in oral ecosystem. Besides the proteases, the CluA receptor or antibody, as well as the exogenous functional domains of CluA and CluA can serve as active ingredients to prevent biofilm development and facilitate biofilm detachment. These enzymes and surface protein adhesin analogues and their receptors are also abundant in other foodborne lactic acid bacteria, including but not limited to, *Streptococcus thermophilus* and Lactobacilli. For example, additional adhesins, HtrA homologs, and cell surface proteinases such as *Streptococcus gordonii* SspA, *Streptococcus mutans* Pac, *Lactobacillus johnsonii* HtrH-like proteinase, *Lactobacillus acidophilus* HtrH-like proteinase, and *Streptococcus thermophilus* exported proteinase can prevent biofilm development and facilitate biofilm detachment. These organisms, as well as their functional components, can be used as active ingredients in the compositions of the present invention. For example, the compositions can be provided in the form of dental hygiene products, including, but not limited to, cheesy tooth masks or gums containing active ingredients, daily wrapped on teeth for certain period of time for treatment, to treat oral biofilms and facilitate their removal.

In addition, a homology of lacto-N-biosidase or beta-N-acetylhexosaminidase (InbA) is also found in *L. lactis* IL1403 genome and *Lactobacillus casei*, making *L. lactis* and other foodborne lactic acid bacteria candidates to remove biofilms that can be directly used in human (Appendix C). These organisms, as well as their functional components, can be used as active ingredients in dental hygiene products, including, but not limited to, cheesy tooth masks or gums containing active ingredients, daily wrapped on teeth for certain period of time for treatment, to treat oral biofilms and facilitate their removal. It will be understood that these bacteria, bacteria bioengineered to express the proteins and/or proteinases of interest, and the proteins or proteinases of interest themselves can be used in the compositions and methods of the present invention. It will be further understood that the compositions and methods of the present invention can be used to treat biotic and abiotic biofilms. These biofilms may be found in the human body, in industrial settings, and/or in residential settings. It will also be understood that the compositions and methods can be selected to at least partially remove a particular biofilm or at least partially prevent the formation of a particular biofilm. Not only the microorganisms expressing the active ingredients but also the active ingredients alone or in abiotic matrixes such as magnetic beads or glass beads and any suitable methods of immobilization, can also be used in compositions and methods for biofilm prevention and/or removal.

FIG. 14 illustrates one of the biofilm interfering working mechanisms. The mechanism is based on a number of roles of particular proteins and proteinases in biofilm formation and detachment. For example, surface adhesins are believed to play a role in microbial biofilm development. Adhesins may act to inter-connect the cells and to stabilize the biofilm structure in hydrodynamic biofilm systems. It is believed that modification of the surface adhesins can affect the shape and

structure of the formed biofilm. It is further believed that cell-cell adherence is a key player in determining the maturation and shape of biofilm.

Certain *Staphylococcus aureus* strains carry a cell wall-associated, 2276-aa biofilm-associated protein (Bap). Bap is involved in *Staphylococcus* pathogenesis, and all isolates carrying Bap are strong biofilm producers. The staphylococcal clumping factors ClfA and ClfB are fibrinogen-binding proteins, and ClfA mediates staphylococcal adherence to host extracellular matrix components as well as abiotic surfaces. Many cell surface proteins involved in adherence, such as Esp, Bap and ClfA, contain core domains with tandem repeats which may be essential for attachment to surfaces or host components. Many of the cell surface proteins are covalently anchored to the cell wall peptidoglycan and possess a carboxyl-terminal LPXTG sequence motif. An enzyme (sortase) is involved in cleaving the LPXTG sequence and covalently attaching the surface protein with C-terminal LPXT to cell wall peptidoglycan.

Co-aggregation describes the phenotype of cell aggregation caused by mixing a strain carrying the adhesin and another pairing strain carrying the cognate receptor. If a bacterial strain carries both the adhesin and the cognate receptor, cell clumping or self-aggregation often occur. Cell surface adhesin-receptor mediated interaction plays an essential role in recruiting compatible organisms for ecosystem expansion. For instance, the *Streptococcus gordonii* surface antigens SspA and SspB are known to mediate coaggregation with other oral bacteria. Certain surface components such as the staphylococcal biofilm-accumulation-associated protein (AAP) have greater impact on Bfm than other adhesins. Staphylococcal strains expressing AAP produce significantly larger amounts of biofilm than strains without this antigen. In *L. lactis*, the clumping protein CluA can also considerably facilitate biofilm development. Biofilm formed by lactococcal strain with induced over-expression of the clumping protein CluA is 7-8 times thicker than without.

Besides adhesins, the involvement of autolysins in biofilm formation is believed to occur in several bacteria. The *S. epidermidis* major autolysin AtlE is a multidomain protein composed of an N-terminal signal peptide, a propeptide (PP), an amidase domain, three highly cationic repeats, and the glucosaminidase domain. In addition to the signal peptide processing, AtlE is also processed by an extracellular protease. Partial processing of AtlE generates degraded products of various sizes. The atlE mutant by transposon mutagenesis is defective in primary adhesion to polystyrene. Although atlE mutation does not have a major impact on cell viability, the cell separation after division is severely impaired, which leads to cell clusters due to covalent interlinking among cells.

It is further believed that extracellular proteolytic enzymes may have roles in biofilm formation. For example, in *Bacillus subtilis*, extracellular proteases appear to be essential for swarming motility, a feature related to the strain's biofilm formation capability. It is believed that protease activities may be essential for proper biofilm formation.

Lactococci are fastidious organisms with multiple amino acid auxotrophies. An efficient proteolytic system to degrade and transport exogenous proteins and peptides is essential for these organisms to grow on their natural habitat rich in protein substrates such as meat, milk and vegetables. The *L. lactis* proteolytic system contains several functional components, including the cell wall associated serine proteinase PrtP and its maturation protein PrtM, the oligopeptide transport system (Opp), intracellular peptidases, di-, tri-peptidases, and di-, tri-peptide transport systems. The proteinase PrtP and the maturation protein PrtM have been identified



associated with plasmids in many lactococcal strains and both plasmid- and chromosomal-located Opp system has been reported. PrtP from different strains may vary in the milk protein casein hydrolyzing specificity. It is believed that PrtP is also involved in processing cell surface proteins.

An HtrA homolog is also believed to be a general cell surface protease of certain lactococcal strains. HtrA is a stress-inducible cell envelope protease with confirmed role in housekeeping in *E. coli*. It is a serine protease and is induced and believed essential for growth at high temperature. Lactococcal HtrA is essential for growth at very high temperatures and is involved in surface proteolysis. Under normal growth conditions, the lactococcal surface protease HtrA is involved in abnormal protein degradation, pro-peptide processing and native protein maturation.

## EXAMPLES

### Example 1

To confirm the role of CluA in lactococcal biofilm formation, the *cluA* gene was cloned into the expression vector pMSP3535, downstream of the *nisA* promoter. The recombinant plasmid was electroporated into ML3 and LM2301, and the transformants were designated HL3A and HL2301A, respectively. The expression of CluA protein in these strains was induced by external nisin signal and confirmed by SDS-PAGE (data not shown). Strains HL3A and HL2301A both exhibited cell aggregation with nisin induction. SEM study showed that both strains also exhibited enhanced Bfm with nisin induction in comparison with the non-induced cultures (FIG. 14 and FIG. 15). Confocal laser scanning microscopy illustrated that the Bfm by CluA-expressed HL3A with nisin induction was 7-8 times thicker than that by the same strain without induction (data not shown). These results confirmed that CluA was the clumping factor, and strongly supported our hypothesis that CluA is a key element in lactococcal Bfm. Increased expression of CluA, triggered by the conjugation event in *L. lactis*, facilitated lactococcal biofilm formation.

Despite the fact that clumping HL2301A (expressing of CluA) developed a 3-dimensional biofilm structure with nisin induction, which was absent by the same strain without the inducer (FIG. 15A-B), the biofilm structure was more localized colonies instead of a well developed network as illustrated by HW002 (FIG. 11E-F) and HL3A (FIG. 14A-B). With HW002, we consistently observed the attachment of the cell clumps to the surface, followed by the rapid expansion of cell clumps into a connected network. A striking feature of HW002 and HL3A is that they form thick biofilms, but these biofilms are easily detached as sheets from the surface of microtiter plates (FIG. 16). Since the only difference between HW002 and HL2301A are the genes encoded by pSK08 and pRS01, the data suggested that other than CluA, pSK08 and pRS01 carry additional Bfm factor(s) that also contributed to proper biofilm growth to detachment.

### Example 2

#### Roles of Exogenous Protease and Protease Inhibitor on *L. lactis* Biofilm Development

The difference in biofilm growth and detachment observed between the CluA-producing strains HL2301A and HW002 shared certain similarity with the biofilm phenotypes of *A. actinomycetemcomitans* strains due to the mutation in the dispersin B gene (*dspB*). As outlined in the literature, a group of macromolecules with the potential to affect biofilm devel-

opment but has not been explored in *L. lactis* are proteases located on the cell surface. Because cell surface proteins play a key role in lactococcal Bfm, proteolytic systems could be involved in processing proteinaceous cell surface component(s) that are essential for Bfm. Indeed both PrtP and its maturation protein PrtM are located on pRS01. Although PrtP is known as the major proteinase involved in breaking down the milk protein casein to support the growth of the microorganisms, evidence showed that PrtP also affected autolysin AcmA activity, which was a Bfm attribute. Therefore it is plausible that cell surface protease PrtP may not only be essential for nutrient supply, but are also involved in processing other cell surface proteins, including those essential for Bfm, from growth to detachment.

To investigate the potential involvement of protease in lactococcal Bfm, biofilm formation by the pSK08 and pRS01-containing strains ML3 and HW002 at the presence and absence of proteinase K and the serine protease inhibitor PMSF was examined. Ten ml of overnight cultures of lactococcal strains ML3 and HW002 were collected by centrifugation, and the cell pellets were resuspended in 1 ml of 100 mM NaH<sub>2</sub>PO<sub>3</sub> (pH 7.0). One hundred  $\mu$ l of the cell suspension was inoculated into 1 ml of M17-L broth in each well of the 24-well microtiter plate. Serially diluted proteinase K and the serine protease inhibitor PMSF were added to the media to investigate the protease dose effect on Bfm. The mixtures were incubated at 30° C. for 5 h. As showed in FIG. 12, at the presence of 2 mg or 1 mg of proteinase K, HW002 cell clumps do not attach to the surface and no biofilm is observed; with 400  $\mu$ g or 200  $\mu$ g of proteinase K, a sheet of biofilm on the surface can be observed, and the increase of the attachment intensity corresponds to decreased concentration of proteinase K. Without exogenous protease, HW002 forms thick biofilm but the biofilm still can be detached from the surface by a simple rinse. The more the protease inhibitor PMSF present in the medium, the tighter the biofilm attached to the surface. Strain ML3 exhibited similar phenomenon except that the biofilm formed was much thinner than that by HW002 (data not shown). These data strongly indicate that lactococcal protease activity has a key role in the facilitated biofilm growth and detachment.

### Example 3

#### Presence of Endogenous Proteases in *L. lactis*

Using *prtP* and *htrA* specific primer pairs [5'AAAGTTCAGCAGCAAG3' (SEQ ID NO: 11) (*prtF*), 5'CCGGCAGTTTGTGGGTG3' (SEQ ID NO: 12) (*prtR*), 5'GGCAAAGCTAATATAGG3' (SEQ ID NO: 13) (*htrA* RTF), 5'GTATTGACATTTACCG3' (SEQ ID NO: 14) (*htrA* RTR)] the presence of *prtP* and *htrA* in ML3, LM2301 and HW002 was examined. The PCR results clearly showed the presence of *htrA* in all three strains and *prtP* in ML3, HW002 and absent in LM2301 (data not shown).

### Example 4

#### Homology of CluA

Homology search of CluA amino acid sequences (GI: 1351100) against the GenBank database revealed that it has significant sequence homology (50% or greater similarity, 30% or greater identity) with regions of genes encoding various surface proteins (antigens) including SpaA from *Streptococcus downei* (*sobrinus*), PaaA from *S. criceti*, surface antigen I/II Pas of *S. intermedius*, salivary agglutinin receptor

## 11

precursor of *S. sanguis* (*sanguinis*), SspA, SspB, Ssp-5 of *S. gordonii*, SpaP, surface antigen I/II precursor, surface antigen Pac, saliva-interacting protein precursor of *S. mutans*, Pac protein homolog/SpaA protein homolog of *S. oralis*, agglutinin receptor of *S. agalactiae*, cell surface protein B of *S. salivarius*. Since many oral streptococci also carry the receptors for these adhesins as evidenced by the auto-aggregation phenotype exhibited in strains such as *S. mutans* UA159 and *S. gordonii* DL1, there is a possibility that the lactococcal adhesin and receptors may cross-react with those in streptococci. Therefore, lactococci have the potential to be involved in the oral ecosystem through adhesin-receptor interaction with the oral microbial residents.

## Example 5

Lactococcal Cells Facilitate Detachment of Biofilms Formed by *Staphylococci*

Overnight cultures of *L. lactis* HW002 and LM2301 were added to a 48 h-biofilm by *Staphylococcus* spp. HLZ and incubated at 30° C. for 2 h. The biofilm residues were examined using the crystal violet rapid assessment assay. FIG. 13 showed that most of the staphylococcal biofilms were removed by co-incubation with HW002. LM2301 also helped detaching the biofilm but the efficiency was much lower than HW002. These results suggest that lactococcal strains carry functional element(s) that can facilitate staphylococcal biofilm removal. However the activity by the plasmid-cured strain LM2301 is much less than HW002, which contains both pRS01 and pSK08.

## Example 6

## Examination of Effect of Casein, Proteinase, and PMSF on Biofilm Formation of Various Lactococcal Strains

The cells of over night cultures of lactococcal strains were collected by centrifugation and resuspended in M17 broth. The cultures were inoculated into 24-well microtiter plate wells with 1 vol of fresh M17 broth. Designated amount of exogenous casein, proteinase and proteinase inhibitor PMSF were added to the culture. All samples were incubated at 30 C for 24 h. The biofilms attached to the surface were rinsed with PBS, fixed with formaldehyde and dehydrated as described previously (Luo et al., 2005) and subjected to Scanning Electron Microscopy analysis.

*Lactococcus lactis* LM2302: plasmid cured strain is shown in FIGS. 17A-E. FIG. 17A is the control. FIGS. 17B-C are with casein. FIGS. 17D-E are with proteinase. FIGS. 17F-G are with PMSF. SK11-1 is a plasmid cured derivative of SK11 and results are shown in FIGS. 18A-H. FIGS. 18A-B are the control. FIGS. 18C-D are with casein. FIGS. 18E-F are with PMSF. FIGS. 18G-H are with proteinase. SK11 is a parental strain that carries multiple plasmids including those encoding for proteinases PrtP and PrtM and results are shown in FIGS. 19A-G. FIG. 19A-B are the control. FIGS. 19C-D are with casein. FIGS. 19E-F are with PMSF. FIG. 19G is with proteinase. The overall biofilm development of SK11 is faster than for the other two strains. Adding casein can enhance the biofilm development. Inhibiting the proteinase activity by PMSF can also facilitate the development of a biofilm structure. Adding proteinase on the other hand slows the development of the network as illustrated in FIGS. 17D-E and FIGS.

## 12

18G-H. In the case of SK11, proteinase just reduced the thickness of the biofilm as shown in FIG. 19G.

## Prophetic Examples

## Prophetic Example 1

## Clone and Express of prtP

The DNA fragment containing the prtP and prtM genes (75) will be cloned into the nisin inducible vector pMSP3535 and the recombinant plasmid pMSP3535CluA (downstream of cluA). These plasmids will be electroporated into LM2301. Bfm of HL2301CluA (preliminary study), HL2301CluAPrtMP and HL2301PrtMP will be examined using the crystal violet staining method and confirmed with SEM. We anticipate HL2301CluAPrtMP will be comparable in Bfm to HW002. The comparison among Bfm by HL2301PrtMP, ML2301, HL2301CluA and HL2301CkuAPrtMP will illustrate whether PrtP by itself is sufficient or it has to work coordinately with CluA to enhance lactococcal biofilm development. PrtP crude extract can be obtained by incubating *L. lactis* strains in Ca<sup>2+</sup> free buffer. However, purified PrtP is required to study the function of PrtP without the interference by other proteins in the crude extract. Thus, we will make a prtP construct using the vector pMSP3535 where a hexahistidine metal-binding site is included for easy purification purpose. The 6× His-tag will be introduced into the C-terminus of PrtP (around position 1127, associated with membrane attachment) using the approaches as described for constructing the CluA secretion plasmid (65). The catalytic domain of PrtP is located near the N-terminus. Therefore the engineered PrtP will retain the catalytic activity but more enzyme molecules will be released to the medium instead of attaching to the membrane. After purification, the His-tag can be cleaved from the recombinant protein by thrombin. A similar construct for secreted CluA has already been made in *E. coli* in our laboratory. Thus, we are fully capable of making this type of constructs. This pMSP3535PrtPHis will be electroporated into ML3 that carries the functional maturation protein PrtM, and consequently the recombinant PrtP precursor can be processed by the PrtM in the host for full activity. The expression of the recombinant PrtP by transformant ML3HisPrtP will be induced by nisii. PrtP will further be isolated and purified by the Ni-affinity column. The expression level and purity of the recombinant protein PrtA will be verified by SDS-PAGE.

## Prophetic Example 2

## Construct prtP Knockout Mutant and Examine its Bfm

Restoration of comparable Bfm in HL2301CluA by the cloned prtP gene would indicate that PrtP is an important player in Bfm. To examine whether other factors (besides CluA and PrtP) encoded by pSK08 and pRS01 may also have an effect on Bfm, we will construct prtP knockout mutant and examine the impact of the mutation on Bfm. The lactococcal suicide plasmid pTRK28 derivative pTRK146 (59), will be used to construct the mutant. An internal fragment of prtP will be amplified by PCR and cloned into pTRK146. The recombinant plasmid will be electroporated into *E. coli* host strain DH5a and the Cm-resistant transformant will be selected. The plasmid p002DPrtP will be extracted from the transformant and then be electroporated into HW002, and the Em-resistant transformant HW002DPrtP will be isolated on M17-Em

plate. Because pTRK146 does not carry the Gram-positive replication of origin and the fragment containing the IS element was deleted from pTRK28, the most likely event when the resistance gene is expressed is due to a cross-over inserting the plasmid p002DPrtP into the chromosomal DNA via homologous recombination. This strategy has been successfully used to knockout the *htrA* gene (56). The successful insertion of the plasmid into the *prtP* gene will be confirmed by PCR using one primer derived from the *Em* gene and the other primer from the upstream sequence from the inserted *prtP* fragment, or Southern hybridization using the *prtP* gene fragment as the probe. The transformant HW002DPrtP will be evaluated for Bfm. If HW002DPrtP exhibits a similar Bfm phenotype as HL2301 CluA, it will suggest that PrtP is the sole factor missing in HL2301 CluA for the facilitated biofilm growth and detachment as observed in HW002. If HW002DPrtP exhibits stronger biofilm network formation than HL2301 CluA but still less than HW002, it will indicate that there are additional factor(s) encoded by pRS01 and pSK08 that contribute to Bfm. If the *prtP* knockout mutant exhibits stronger Bfm than HW002, it will suggest that PrtP is likely only involved in biofilm detachment, and some other factor(s) are involved in biofilm growth.

To further confirm the linkage between the gene and the phenotype, the plasmid p002DPrtP (Lac+Prt-Emr) will further be transferred to the tetracycline-resistant derivative of LM2301, designated HL2301Tet, by conjugation. The Bfm of the transconjugate will be examined. We anticipate that the Bfm phenotype will also be transferable to HL2301Tet. In our preliminary study, we have already demonstrated that CluA is the clumping factor and a biofilm attribute, but is not a major player in high frequency gene transfer (49). If the recombinant plasmid can be transmitted by conjugation, we will compare the difference in conjugation frequencies between the mating pair A (HW002×HL2301Tet) and mating pair B (HW002DPrtP×HL2301Tet). If pair B has similar frequency as pair A, it will suggest that PrtP does not have an effect on high frequency gene transfer. If pair B has a transfer frequency lower than pair A, it will indicate that PrtP also has a role in high frequency gene transfer, besides Bfm. If we fail to obtain transconjugants due to the *prtP* knockout, we will isolate the plasmid p002DPrtP and electroporated into HL2301Tet and examine the Bfm of the transformant, to confirm that the Bfm phenotype due to PrtP can be illustrated outside its original host.

### Prophetic Example 3

#### Determine the Role of PrtP in Lactococcal Bfm

To assess the role of PrtP in Bfm, exogenous enzyme will be added to HL2301CluA to examine the Bfm complementation. Purified PrtP (10 mg, 50 mg, 100 mg, and 500 mg, respectively) will be added to 1.5 ml of M17-G broth in microtiter plate wells inoculated with HL2301 CluA (10% overnight culture) at the presence of nisin, and incubated at 30° C. Bfm at 4, 8, and 24 h will be evaluated. We expect to observe restoration of the rapid Bfm growth and detachment phenotype as exhibited by HW002 with higher concentration of exogenous PrtP. With lower concentration of PrtP, biofilm will be attached to the surface of the microtiter plate wells more tightly. We particularly anticipate to observe the biofilm phenotype difference between HL2301CluA (colonies or spots) without PrtP, and the ones with low dose PrtP (biofilm network), which will suggest the role of PrtP in biofilm growth. It is anticipated that biofilm will detach with high dose of PrtP. If this dose effect is observed, it will support the

hypothesis that only one enzyme (PrtP) is enough to do the trick. If the dose effect in HL2301CluA is not observed, and exogenous PrtP can only facilitate biofilm detachment by HW002, it will suggest the involvement of additional factor(s) in forming the biofilm network. To further assist understanding of the actual function of PrtP in Bfm, we will examine the potential of PrtP serving as a general protease in processing other cell surface components (besides AcmA) involved in Bfm. Particularly, we will assess whether PrtP can hydrolyze the major surface protein CluA. We will prepare secreted lactococcal CluA using the approach as described by Stentz et al. (2004). Basically, the CluA C-terminus membrane anchor LPXTG will be replaced by a hexahistidine metal-binding site, and the recombinant protein will be secreted to the media instead of attaching to the cell wall. Meanwhile, the His-tagged protein can be purified by Ni-affinity column. Using the primer pair TGTGGGCCCTTT-TAAATGGGCAG (SEQ ID NO: 15) and GAGATCTCTAATGATGATGATGATGAT-GAACCTCTTGGGACAAGTGAACCTGT-GATTTTTTCAATCACG (SEQ ID NO: 16), we have amplified and cloned the *cluA* fragment into the TA cloning vector (Invitrogen Co., CA) in *E. coli*. We will further digest and clone the fragment into pMSP3535, in which the expression of the recombinant DNA in lactococci can be induced by nisin. The recombinant plasmid pMS3535CluAHis will be electroporated into LM2301. The synthesis of the recombinant CluA protein will be induced by nisin, and CluA will be isolated and purified by Ni-column following procedures as described previously (65). The expression and purity of the recombinant protein CluA will be verified by SDS-PAGE. The fusion protein will then be sent to Affinity BioReagents (Golden, Colo.) for polyclonal antibody preparation. Purified PrtP (500 mg, 200 mg, 20 mg, 5 mg, respectively), prepared as described previously, will be added to 500 mg of CluA solution in 10 mM Tris buffer (pH 7.0) and incubated at 30° C. for 1 h. The hydrolyzed products are subject to Western Blot analysis using the CluA antibody. Reactions without PrtP or with PMSF will be included as controls. We anticipate to detect multiple CluA degradation products, which will indicate the involvement of PrtP in CluA processing. At the presence of PMSF the proteolytic degradation will be inhibited. This result will suggest the involvement of PrtP in Bfm as a more general protease hydrolyzing multiple surface Bfm factors such as CluA. If CluA degradation products are not detected, it will suggest that PrtP has a rather specific spectrum to process certain surface proteins such as AcmA, and further studies are needed to assess the exact mechanism of PrtP in Bfm.

### Prophetic Example 4

#### Investigate the Potential Involvement of HtrA in Bfm

Our preliminary data showed that LM2301 can also remove staphylococcal biofilm, although at a scale much lower than HW002. This result indicated the possible involvement of a chromosomal factor in Bfm. The stress responsive HtrA is the second surface proteolytic system identified in lactococci. Our preliminary data showed that all the lactococcal strains tested contain the *htrA* gene. Because of its contribution to stress response and its role in processing secreted proteins, HtrA is considered another potential candidate having a role in Bfm. To test this possibility, we will examine the contribution of HtrA to Bfm using similar approaches described above for PrtP. We will amplify by PCR the *htrA* gene, clone it into pTRK146 and construct the *htrA* knockout

suicide plasmid pHWDHtrA. The recombinant plasmid will be maintained in *E. coli* and electroporated into HW002, ML3 and LM2301. The Em-resistant transformants will be confirmed by PCR or Southern hybridization for the proper insertion of the plasmid into the *htrA* gene. The transformants will be evaluated for both growth and viability in M17-G or M17-L, broth at 30° C. and 39° C. Bfm by these strains will also be evaluated, with the expectation that Bfm by LM2301 and LM2301DHtrA will be much slower than that by HW002, ML3 and their mutants. We anticipate that overall *htrA* mutant strains will be comparable to the wild-types at 30° C., but impaired at 39° C. for both growth and viability in M17 broth. The Bfm difference between the mutants HW002DHtrA, ML3DHtrA and the wild-type strains will illustrate the involvement of HtrA in lactococcal Bfm. It is a common phenomenon that inactivating one protease may trigger over-expression of other proteases in the microbe. Therefore we will also monitor the expression level of *htrA* in the *prtP* knockout mutants and vice versa by RT-PCR, using procedures described in our recent publication. The Bfm phenotypic difference between *htrA* mutants and *prtP* mutants will further reveal potential difference in functions among the two proteolytic systems. We will also clone the *htrA* gene into pMSP3535CluA downstream of the *cluA* gene. The recombinant plasmid pMSP3535CluAHtrA will be electroporated into LM2301. If the transformant does not restore Bfm phenotype as exhibited by HW002, it will indicate a less significant or no role of HtrA in lactococcal Bfm. If the transformant restored Bfm phenotype as HW002, it will suggest that HtrA is required for Bfm. Since HtrA is a stress responsible surface protease and is widely distributed in Gram-positive and Gram-negative bacteria, demonstration of its role in lactococcal Bfm would imply that such a protease may have a universal role in Bfm. The controlled expression of HtrA could therefore be a key process in biofilm development from initiation to detachment. If HtrA is found to be involved in Bfm, we will follow up with a new proposal using microarray to identify molecular elements and the potential network involved in Bfm under stress conditions (39° C. versus the control at 30° C.).

#### Prophetic Example 5

##### Examine the Efficacy of CluA Antibody and CluA Protein in Interfering Lactococcal Clumping and Bfm

The preparation of CluA and CluA antibody has been achieved. To determine the efficacy of CluA polyclonal antibody on interrupting biofilms, we will harvest cells from overnight cultures of HL2301CluA (nisin induced) and HW002 by centrifugation, and the cells will be resuspended in 1/10 vol of 100 mM NaH<sub>2</sub>PO<sub>4</sub> buffer. Then 0.5 ml of the cell suspension will be inoculated into 1 ml of M17 broth in microtiter plate wells. The CluA antibody will be serially diluted and mixed with the inoculated cells, and the mixture will be incubated at 30° C. for 4 h. Disruption of lactococcal cell clumps and Bfm by the various titers of CluA antibodies will be assessed using the rapid crystal violet staining assay. We anticipate that CluA antibody above a threshold level will minimize HL2301CluA cell clumping and Bfm by blocking the cell-cell interaction between the adhesin and receptor. Besides CluA antibody, incubating the cell suspension with CluA protein will have similar effect. We expect that cell mobility will rise with the increased concentrations of exogenous CluA, and high concentration of CluA will completely interrupt cell clumping and Bfm. Since such strategy has been

proved to be effective in other organisms, the likelihood of success in the lactococcal system is expected to be high.

#### Prophetic Example 6

##### Identify Pairing Oral Streptococci Cross-reacting with Lactococcal Surface Antigen(s)

Certain streptococcal strains, such as *S. mutans* UA159 and *S. gordonii* DL1, express both the adhesins and the cognate receptors at high levels and therefore exhibit auto-aggregation. CluA shares significant sequence homology with major adhesins in both organisms. To test the cross-reactivity between lactococcal and streptococcal surface components, we will harvest overnight cultures of UA 159 and DL1 and resuspend the cell pellets in Tris-HCl buffer (pH 6.8). Serially diluted exogenous CluA or CluA antibody will be added to the cell aggregation suspensions and mixed by vortex. We expect to observe the dissociation of the streptococcal cell clumps due to the competitive binding between CluA-streptococcal receptor or CluA antibody-streptococcal adhesin, similar to those illustrated in FIGS. 9a and 9b. This result will suggest the cross-reactivity between the lactococcal and streptococcal surface components. For those strains that do not exhibit auto-aggregation, we will use (with some modification) the cell coaggregation test (Kolenbrander and Andersen, 1990) to select for streptococcal strains with CluA-compatible receptors. Because *L. lactis* ML3 and its derivatives carry the CluA receptor, over-expression of CluA in these strains results in auto-aggregation. Therefore, these strains cannot be used to screen for streptococcal strains by the co-aggregation test. We will construct a surrogate *Bacillus subtilis* strain where pMSP3535CluA will be introduced into *B. subtilis* strain IG-20 by natural transformation. The CluA over-expression is induced by nisin induction and expression of the CluA in *Bacillus* will be verified by Western Blot analysis using the CluA antibody. The functionality of the nisin genes in *Bacillus* has been demonstrated previously and therefore it is technically feasible to construct the surrogate strain HLbsCluA. HLbsCluA cells (after nisin induction) will be used in the coaggregation assay to screen for streptococcal strains with CluA-compatible receptor(s) following the well-established procedures by others.

#### Prophetic Example 7

##### Investigate the Role of Lactococcal Functional Components in Dispersing Streptococcal Biofilms

Pairing streptococcal strains identified above are subject to biofilm disruption study. Biofilms will be cultivated in 24-well polystyrene microtiter plates using procedures established in our laboratory with modifications, by inoculating cultures in SDM medium and incubating the culture at 37° C. with 5% CO<sub>2</sub> for 24-48 h without agitation (43). Serially diluted functional lactococcal components CluA, CluA antibody, PrtP, respectively, will be added to individual wells containing the streptococcal biofilms and incubated at 37° C. for 2-4 h. Biofilm detachment will be assessed by the crystal violet staining assay. We anticipate positive roles of these components in negate oral streptococcal Bfm. To further assess the efficacy of lactococcal strains in detaching streptococcal biofilms, we will harvest cells from overnight cultures of HW002, ML3 and LM2301 by centrifugation. The cells will be resuspended in 1/10 volume of coaggregation buffer (1 mM Tris, pH 8.0, 150 mM NaCl, 0.1 mM CaCl<sub>2</sub>, 0.1 mM MgCl<sub>2</sub>, 0.02% Na<sub>3</sub>N). One hundred ml of the cell sus-

pension will be added to each microtiter plate well containing the streptococcal biofilms. The mixture will be incubated at 37° C. with 5% CO<sub>2</sub> for 10 min, 30 min and 1 h. Biofilms will be rinsed once with water and the biofilm residues will be assessed by the crystal violet staining assay. It is anticipated that the lactococcal strains will facilitate streptococcal biofilm removal, and strains carry multiple functional components such as HW002 will have the most prominent effect. If successful, this could serve as a prototype in developing dental hygiene products such as live culture-containing cheesy paste or mask for routine home treatment.

The present invention should not be considered limited to the specific examples described above, but rather should be understood to cover all aspects of the invention. Various modifications, equivalent processes, as well as numerous structures and devices to which the present invention may be applicable will be readily apparent to those of skill in the art.

It will be obvious to those skilled in the art that various changes may be made without departing from the scope of the invention, which is not to be considered limited to what is described in the specification.

---

 SEQUENCE LISTING
 

---

<160> NUMBER OF SEQ ID NOS: 41

<210> SEQ ID NO 1

<211> LENGTH: 408

<212> TYPE: PRT

<213> ORGANISM: *Lactococcus lactis*

<400> SEQUENCE: 1

```

Met Ala Lys Ala Asn Ile Gly Lys Leu Leu Leu Thr Gly Val Val Gly
 1           5           10
Gly Ala Ile Ala Leu Gly Gly Ser Ala Ile Tyr Gln Ser Thr Thr Asn
 20           25           30
Gln Ser Ala Asn Asn Ser Arg Ser Asn Thr Thr Ser Thr Lys Val Ser
 35           40           45
Asn Val Ser Val Asn Val Asn Thr Asp Val Thr Ser Ala Ile Lys Lys
 50           55           60
Val Ser Asn Ser Val Val Ser Val Met Asn Tyr Gln Lys Asp Asn Ser
 65           70           75           80
Gln Ser Ser Asp Phe Ser Ser Ile Phe Gly Gly Asn Ser Gly Ser Ser
 85           90           95
Ser Ser Thr Asp Gly Leu Gln Leu Ser Ser Glu Gly Ser Gly Val Ile
 100          105          110
Tyr Lys Lys Ser Gly Gly Asp Ala Tyr Val Val Thr Asn Tyr His Val
 115          120          125
Ile Ala Gly Asn Ser Ser Leu Asp Val Leu Leu Ser Gly Gly Gln Lys
 130          135          140
Val Lys Ala Ser Val Val Gly Tyr Asp Glu Tyr Thr Asp Leu Ala Val
 145          150          155          160
Leu Lys Ile Ser Ser Glu His Val Lys Asp Val Ala Thr Phe Ala Asp
 165          170          175
Ser Ser Lys Leu Thr Ile Gly Glu Pro Ala Ile Ala Val Gly Ser Pro
 180          185          190
Leu Gly Ser Gln Phe Ala Asn Thr Ala Thr Glu Gly Ile Leu Ser Ala
 195          200          205
Thr Ser Arg Gln Val Thr Leu Thr Gln Glu Asn Gly Gln Thr Thr Asn
 210          215          220
Ile Asn Ala Ile Gln Thr Asp Ala Ala Ile Asn Pro Gly Asn Ser Gly
 225          230          235          240
Gly Ala Leu Ile Asn Ile Glu Gly Gln Val Ile Gly Ile Thr Gln Ser
 245          250          255
Lys Ile Thr Thr Thr Glu Asp Gly Ser Thr Ser Val Glu Gly Leu Gly
 260          265          270
Phe Ala Ile Pro Ser Asn Asp Val Val Asn Ile Ile Asn Lys Leu Glu
 275          280          285

```

-continued

---

Ala Asp Gly Lys Ile Ser Arg Pro Ala Leu Gly Ile Arg Met Val Asp  
 290 295 300

Leu Ser Gln Leu Ser Thr Asn Asp Ser Ser Gln Leu Lys Leu Pro Ser  
 305 310 315 320

Ser Val Thr Gly Gly Val Val Val Tyr Ser Val Gln Ser Gly Leu Pro  
 325 330 335

Ala Ala Ser Ala Gly Leu Lys Ala Gly Asp Val Ile Thr Lys Val Gly  
 340 345 350

Asp Thr Ala Val Thr Ser Ser Thr Asp Leu Gln Ser Ala Leu Tyr Ser  
 355 360 365

His Asn Ile Asn Asp Thr Val Lys Val Thr Tyr Tyr Arg Asp Gly Lys  
 370 375 380

Ser Asn Thr Ala Asp Val Lys Leu Ser Lys Ser Thr Ser Asp Leu Glu  
 385 390 395 400

Thr Ser Ser Pro Ser Ser Ser Asn  
 405

<210> SEQ ID NO 2  
 <211> LENGTH: 1902  
 <212> TYPE: PRT  
 <213> ORGANISM: Lactococcus lactis

<400> SEQUENCE: 2

Met Gln Arg Lys Lys Lys Gly Leu Ser Phe Leu Leu Ala Gly Thr Val  
 1 5 10 15

Ala Leu Gly Ala Leu Ala Val Leu Pro Val Gly Glu Ile Gln Ala Lys  
 20 25 30

Ala Ala Ile Ser Gln Gln Thr Lys Gly Ser Ser Leu Ala Asn Thr Val  
 35 40 45

Thr Ala Ala Thr Ala Lys Gln Ala Ala Thr Asp Thr Thr Ala Ala Thr  
 50 55 60

Thr Asn Gln Ala Ile Ala Thr Gln Leu Ala Ala Lys Gly Ile Asp Tyr  
 65 70 75 80

Asn Lys Leu Asn Lys Val Gln Gln Gln Asp Ile Tyr Val Asp Val Ile  
 85 90 95

Val Gln Met Ser Ala Ala Pro Ala Ser Glu Asn Gly Thr Leu Arg Thr  
 100 105 110

Asp Tyr Ser Ser Thr Ala Glu Ile Gln Gln Glu Thr Asn Lys Val Ile  
 115 120 125

Ala Ala Gln Ala Ser Val Lys Ala Ala Val Glu Gln Val Thr Gln Gln  
 130 135 140

Thr Ala Gly Glu Ser Tyr Gly Tyr Val Val Asn Gly Phe Ser Thr Lys  
 145 150 155 160

Val Arg Val Val Asp Ile Pro Lys Leu Lys Gln Ile Ala Gly Val Lys  
 165 170 175

Thr Val Thr Leu Ala Lys Val Tyr Tyr Pro Thr Asp Ala Lys Ala Asn  
 180 185 190

Ser Met Ala Asn Val Gln Ala Val Trp Ser Asn Tyr Lys Tyr Lys Gly  
 195 200 205

Glu Gly Thr Val Val Ser Val Ile Asp Ser Gly Ile Asp Pro Thr His  
 210 215 220

Lys Asp Met Arg Leu Ser Asp Asp Lys Asp Val Lys Leu Thr Lys Ser  
 225 230 235 240

Asp Val Glu Lys Phe Thr Asp Thr Val Lys His Gly Arg Tyr Phe Asn  
 245 250 255

-continued

---

Ser Lys Val Pro Tyr Gly Phe Asn Tyr Ala Asp Asn Asn Asp Thr Ile  
 260 265 270  
 Thr Asp Asp Lys Val Asp Glu Gln His Gly Met His Val Ala Gly Ile  
 275 280 285  
 Ile Gly Ala Asn Gly Thr Gly Asp Asp Pro Ala Lys Ser Val Val Gly  
 290 295 300  
 Val Ala Pro Glu Ala Gln Leu Leu Ala Met Lys Val Phe Thr Asn Ser  
 305 310 315 320  
 Asp Thr Ser Ala Thr Thr Gly Ser Asp Thr Leu Val Ser Ala Ile Glu  
 325 330 335  
 Asp Ser Ala Lys Ile Gly Ala Asp Val Leu Asn Met Ser Leu Gly Ser  
 340 345 350  
 Asp Ser Gly Asn Gln Thr Leu Glu Asp Pro Glu Ile Ala Ala Val Gln  
 355 360 365  
 Asn Ala Asn Glu Ser Gly Thr Ala Ala Val Ile Ser Ala Gly Asn Ser  
 370 375 380  
 Gly Thr Ser Gly Ser Ala Thr Glu Gly Val Asn Lys Asp Tyr Tyr Gly  
 385 390 395 400  
 Leu Gln Asp Asn Glu Met Val Gly Thr Pro Gly Thr Ser Arg Gly Ala  
 405 410 415  
 Thr Thr Val Ala Ser Ala Glu Asn Thr Asp Val Ile Thr Gln Ala Val  
 420 425 430  
 Thr Ile Thr Asp Gly Thr Gly Leu Gln Leu Gly Pro Glu Thr Ile Gln  
 435 440 445  
 Leu Ser Ser Asn Asp Phe Thr Gly Ser Phe Asp Gln Lys Lys Phe Tyr  
 450 455 460  
 Val Val Lys Asp Ala Ser Gly Asn Leu Ser Lys Gly Lys Val Ala Asp  
 465 470 475 480  
 Tyr Thr Ala Asp Ala Lys Gly Lys Ile Ala Ile Val Lys Arg Gly Glu  
 485 490 495  
 Leu Thr Phe Asp Asp Lys Gln Lys Tyr Ala Gln Ala Ala Gly Ala Ala  
 500 505 510  
 Gly Leu Ile Ile Val Asn Asn Asp Gly Thr Ala Thr Pro Val Thr Ser  
 515 520 525  
 Met Ala Leu Thr Thr Thr Phe Pro Thr Phe Gly Leu Ser Ser Val Thr  
 530 535 540  
 Gly Gln Lys Leu Val Asp Trp Val Thr Ala His Pro Asp Asp Ser Leu  
 545 550 555 560  
 Gly Val Lys Ile Ala Leu Thr Leu Val Pro Asn Gln Lys Tyr Thr Glu  
 565 570 575  
 Asp Lys Met Ser Asp Phe Thr Ser Tyr Gly Pro Val Ser Asn Leu Ser  
 580 585 590  
 Phe Lys Pro Asp Ile Thr Ala Pro Gly Gly Asn Ile Trp Ser Thr Gln  
 595 600 605  
 Asn Asn Asn Gly Tyr Thr Asn Met Ser Gly Thr Ser Met Ala Ser Pro  
 610 615 620  
 Phe Ile Ala Gly Ser Gln Ala Leu Leu Lys Gln Ala Leu Asn Asn Lys  
 625 630 635 640  
 Asn Asn Pro Phe Tyr Ala Tyr Tyr Lys Gln Leu Lys Gly Thr Ala Leu  
 645 650 655  
 Thr Asp Phe Leu Lys Thr Val Glu Met Asn Thr Ala Gln Pro Ile Asn  
 660 665 670  
 Asp Ile Asn Tyr Asn Asn Val Ile Val Ser Pro Arg Arg Gln Gly Ala  
 675 680 685

-continued

---

Gly Leu Val Asp Val Lys Ala Ala Ile Asp Ala Leu Glu Lys Asn Pro  
 690 695 700

Ser Thr Val Val Ala Glu Asn Gly Tyr Pro Ala Val Glu Leu Lys Asp  
 705 710 715 720

Phe Thr Ser Thr Asp Lys Thr Phe Lys Leu Thr Phe Thr Asn Arg Thr  
 725 730 735

Thr His Glu Leu Thr Tyr Gln Met Asp Ser Asn Thr Asp Thr Asn Ala  
 740 745 750

Val Tyr Thr Ser Ala Thr Asp Pro Asn Ser Gly Val Leu Tyr Asp Lys  
 755 760 765

Lys Ile Asp Gly Ala Ala Ile Lys Ala Gly Ser Asn Ile Thr Val Pro  
 770 775 780

Ala Gly Lys Thr Ala Gln Ile Glu Phe Thr Leu Ser Leu Pro Lys Ser  
 785 790 795 800

Phe Asp Gln Gln Gln Phe Val Glu Gly Phe Leu Asn Phe Lys Gly Ser  
 805 810 815

Asp Gly Ser Arg Leu Asn Leu Pro Tyr Met Gly Phe Phe Gly Asp Trp  
 820 825 830

Asn Asp Gly Lys Ile Val Asp Ser Leu Asn Gly Ile Thr Tyr Ser Pro  
 835 840 845

Ala Gly Gly Asn Phe Gly Thr Val Pro Leu Leu Thr Asn Lys Asn Thr  
 850 855 860

Gly Thr Gln Tyr Tyr Gly Gly Met Val Thr Asp Ala Asp Gly Asn Gln  
 865 870 875 880

Thr Val Asp Asp Gln Ala Ile Ala Phe Ser Ser Asp Lys Asn Ala Leu  
 885 890 895

Tyr Asn Asp Ile Ser Met Lys Tyr Tyr Leu Leu Arg Asn Ile Ser Asn  
 900 905 910

Val Gln Val Asp Ile Leu Asp Gly Gln Gly Asn Lys Val Thr Thr Leu  
 915 920 925

Ser Ser Ser Thr Asn Leu Thr Lys Thr Tyr Tyr Asn Ala His Ser Gln  
 930 935 940

Gln Tyr Ile Tyr Tyr His Ala Pro Ala Trp Asp Gly Thr Tyr Tyr Asp  
 945 950 955 960

Gln Arg Asp Gly Asn Ile Lys Thr Ala Asp Asp Gly Ser Tyr Thr Tyr  
 965 970 975

Arg Ile Ser Gly Val Pro Glu Gly Gly Asp Lys Arg Gln Val Phe Asp  
 980 985 990

Val Pro Phe Lys Leu Asp Ser Lys Ala Pro Thr Val Arg His Val Ala  
 995 1000 1005

Leu Ser Ala Lys Thr Lys Asn Gly Lys Thr Gln Tyr Tyr Leu Thr Ala  
 1010 1015 1020

Glu Val Lys Asp Asp Leu Ser Gly Leu Asp Ala Thr Lys Ser Val Lys  
 1025 1030 1035 1040

Thr Ala Ile Asn Glu Val Thr Asn Leu Asp Ala Thr Phe Thr Asp Ala  
 1045 1050 1055

Gly Thr Thr Ala Asp Gly Tyr Thr Lys Ile Glu Thr Pro Leu Ser Asp  
 1060 1065 1070

Glu Gln Ala Gln Ala Leu Gly Asn Gly Asp Asn Ser Ala Glu Leu Tyr  
 1075 1080 1085

Leu Thr Asp Asn Ala Ser Asn Ala Thr Asp Gln Asp Ala Ser Val Gln  
 1090 1095 1100

Lys Pro Gly Ser Thr Ser Phe Asp Leu Ile Val Asn Gly Ser Gly Ile



-continued

1105	1110	1115	1120
Pro Asp Lys Ile Ser Ser Thr Thr Thr Gly Tyr Glu Ala Asn Thr Gln	1125	1130	1135
Gly Gly Gly Thr Tyr Thr Phe Ser Gly Thr Tyr Pro Ala Ala Val Asp	1140	1145	1150
Gly Thr Tyr Thr Asp Ala Gln Gly Lys Lys His Asp Leu Asn Thr Thr	1155	1160	1165
Tyr Asp Ala Ala Thr Asn Ser Phe Thr Ala Ser Met Pro Val Thr Asn	1170	1175	1180
Ala Asp Tyr Ala Ala Gln Val Asp Leu Tyr Ala Asp Lys Ala His Thr	1185	1190	1195
Gln Leu Leu Lys His Phe Asp Thr Lys Val Arg Leu Thr Ala Pro Thr	1205	1210	1215
Phe Thr Asp Leu Lys Phe Asn Asn Gly Ser Asp Gln Thr Ser Glu Ala	1220	1225	1230
Thr Ile Lys Val Thr Gly Thr Val Ser Ala Asp Thr Lys Thr Val Asn	1235	1240	1245
Val Gly Asp Thr Val Ala Ala Leu Asp Ala Gln His His Phe Ser Val	1250	1255	1260
Asp Val Pro Val Asn Tyr Gly Asp Asn Thr Ile Lys Val Ile Ala Thr	1265	1270	1275
Asp Glu Asp Gly Asn Thr Thr Thr Glu Gln Lys Thr Ile Thr Ser Ser	1285	1290	1295
Tyr Asp Pro Asp Met Leu Lys Asn Pro Val Thr Phe Asp Gln Gly Val	1300	1305	1310
Thr Phe Gly Ser Asn Glu Phe Asn Ala Thr Ser Ala Lys Phe Tyr Asp	1315	1320	1325
Pro Lys Thr Gly Ile Ala Thr Ile Thr Gly Lys Val Lys His Pro Thr	1330	1335	1340
Thr Thr Leu Gln Val Asp Gly Lys Gln Ile Pro Ile Lys Asp Asp Leu	1345	1350	1355
Thr Phe Ser Phe Thr Leu Asp Leu Gly Thr Leu Gly Gln Lys Pro Phe	1365	1370	1375
Gly Val Val Val Gly Asp Thr Thr Gln Asn Lys Thr Phe Gln Glu Ala	1380	1385	1390
Leu Thr Phe Ile Leu Asp Ala Val Ala Pro Thr Leu Ser Leu Asp Ser	1395	1400	1405
Ser Thr Asp Ala Pro Val Tyr Thr Asn Asp Pro Asn Phe Gln Ile Thr	1410	1415	1420
Gly Thr Ala Thr Asp Asn Ala Gln Tyr Leu Ser Leu Ser Ile Asn Gly	1425	1430	1435
Ser Ser Val Ala Ser Gln Tyr Ala Asp Ile Asn Ile Asn Ser Gly Lys	1445	1450	1455
Pro Gly His Met Ala Ile Asp Gln Pro Val Lys Leu Leu Glu Gly Lys	1460	1465	1470
Asn Val Leu Thr Val Ala Val Thr Asp Ser Glu Asp Asn Thr Thr Thr	1475	1480	1485
Lys Asn Ile Thr Val Tyr Tyr Glu Pro Lys Lys Thr Leu Ala Ala Pro	1490	1495	1500
Thr Val Thr Pro Ser Thr Thr Glu Pro Ala Gln Thr Val Thr Leu Thr	1505	1510	1515
Ala Asn Ala Ala Ala Thr Gly Glu Thr Val Gln Tyr Ser Ala Asp Gly	1525	1530	1535

-continued

Gly Lys Thr Tyr Gln Asp Val Pro Ala Ala Gly Val Thr Ile Thr Ala  
 1540 1545 1550  
 Asn Gly Thr Phe Lys Phe Lys Ser Thr Asp Leu Tyr Gly Asn Glu Ser  
 1555 1560 1565  
 Pro Ala Val Asp Tyr Val Val Thr Asn Ile Lys Ala Asp Asp Pro Ala  
 1570 1575 1580  
 Gln Leu Gln Ala Ala Lys Gln Ala Leu Thr Asn Leu Ile Ala Ser Ala  
 1585 1590 1595 1600  
 Lys Thr Leu Ser Ala Ser Gly Lys Tyr Asp Asp Ala Thr Thr Thr Ala  
 1605 1610 1615  
 Leu Ala Ala Ala Thr Gln Lys Ala Gln Thr Ala Leu Asp Gln Thr Asn  
 1620 1625 1630  
 Ala Ser Val Asp Ser Leu Thr Gly Ala Asn Arg Asp Leu Gln Thr Ala  
 1635 1640 1645  
 Ile Asn Gln Leu Ala Ala Lys Leu Pro Ala Asp Lys Lys Thr Ser Leu  
 1650 1655 1660  
 Leu Asn Gln Leu Gln Ser Val Lys Asp Ala Leu Gly Thr Asp Leu Gly  
 1665 1670 1675 1680  
 Asn Gln Thr Asp Pro Ser Thr Gly Lys Thr Phe Thr Ala Ala Leu Asp  
 1685 1690 1695  
 Asp Leu Val Ala Gln Ala Gln Ala Gly Thr Gln Thr Asp Asp Gln Leu  
 1700 1705 1710  
 Gln Ala Thr Leu Ala Lys Ile Leu Asp Glu Val Leu Ala Lys Leu Ala  
 1715 1720 1725  
 Glu Gly Ile Lys Ala Ala Thr Pro Ala Glu Val Gly Asn Ala Lys Asp  
 1730 1735 1740  
 Ala Ala Thr Gly Lys Thr Trp Tyr Ala Asp Ile Ala Asp Thr Leu Thr  
 1745 1750 1755 1760  
 Ser Gly Gln Ala Ser Ala Asp Ala Ser Asp Lys Leu Ala His Leu Gln  
 1765 1770 1775  
 Ala Leu Gln Ser Leu Lys Thr Lys Val Ala Ala Ala Val Glu Ala Asp  
 1780 1785 1790  
 Lys Thr Val Gly Lys Gly Asp Asp Thr Thr Gly Thr Ser Asp Lys Gly  
 1795 1800 1805  
 Ser Gly Gln Gly Thr Pro Ala Pro Ala Thr Gly Asp Thr Gly Lys Asp  
 1810 1815 1820  
 Lys Gly Asp Glu Gly Ser Gln Pro Ser Ser Gly Gly Asn Ile Pro Thr  
 1825 1830 1835 1840  
 Asn Pro Ala Thr Thr Thr Ser Thr Ser Thr Asp Asp Thr Thr Asp Arg  
 1845 1850 1855  
 Asn Gly Gln His Thr Thr Gly Lys Gly Ala Leu Pro Lys Thr Gly Glu  
 1860 1865 1870  
 Thr Thr Glu Arg Pro Ala Phe Gly Phe Leu Gly Val Ile Val Val Ile  
 1875 1880 1885  
 Leu Met Gly Val Leu Gly Leu Lys Arg Lys Gln Arg Glu Glu  
 1890 1895 1900

<210> SEQ ID NO 3  
 <211> LENGTH: 299  
 <212> TYPE: PRT  
 <213> ORGANISM: Lactococcus lactis

<400> SEQUENCE: 3

Met Lys Lys Lys Met Arg Leu Lys Val Leu Leu Ala Ser Thr Ala Thr  
 1 5 10 15

-continued

Ala Leu Leu Leu Leu Ser Gly Cys Gln Ser Asn Gln Thr Asp Gln Thr  
 20 25 30

Val Ala Thr Tyr Ser Gly Gly Lys Val Thr Glu Ser Ser Phe Tyr Lys  
 35 40 45

Glu Leu Lys Gln Ser Pro Thr Thr Lys Thr Met Leu Ala Asn Met Leu  
 50 55 60

Ile Tyr Arg Ala Leu Asn His Ala Tyr Gly Lys Ser Val Ser Thr Lys  
 65 70 75 80

Thr Val Asn Asp Ala Tyr Asp Ser Tyr Lys Gln Gln Tyr Gly Glu Asn  
 85 90 95

Phe Asp Ala Phe Leu Ser Gln Asn Gly Phe Ser Arg Ser Ser Phe Lys  
 100 105 110

Glu Ser Leu Arg Thr Asn Phe Leu Ser Glu Val Ala Leu Lys Lys Leu  
 115 120 125

Lys Lys Val Ser Glu Ser Gln Leu Lys Ala Ala Trp Lys Thr Tyr Gln  
 130 135 140

Pro Lys Val Thr Val Gln His Ile Leu Thr Ser Asp Glu Asp Thr Ala  
 145 150 155 160

Lys Gln Val Ile Ser Asp Leu Ala Ser Gly Lys Asp Phe Ala Met Leu  
 165 170 175

Ala Lys Thr Asp Ser Ile Asp Thr Ala Thr Lys Asp Asn Gly Gly Lys  
 180 185 190

Ile Ser Phe Glu Leu Asn Asn Lys Thr Leu Asp Ala Thr Phe Lys Asp  
 195 200 205

Ala Ala Tyr Lys Leu Lys Asn Gly Asp Tyr Thr Gln Thr Pro Val Lys  
 210 215 220

Val Thr Asp Gly Tyr Glu Val Ile Lys Met Ile Asn His Pro Ala Lys  
 225 230 235 240

Gly Thr Phe Thr Ser Ser Lys Lys Val Leu Thr Ala Ser Val Tyr Ala  
 245 250 255

Lys Trp Ser Arg Asp Ser Ser Ile Met Gln Arg Val Ile Ser Gln Val  
 260 265 270

Leu Lys Asn Gln His Val Thr Ile Lys Asp Lys Asp Leu Ala Asp Ala  
 275 280 285

Leu Asp Ser Tyr Lys Lys Leu Ala Thr Thr Asn  
 290 295

<210> SEQ ID NO 4  
 <211> LENGTH: 1243  
 <212> TYPE: PRT  
 <213> ORGANISM: Lactococcus lactis

<400> SEQUENCE: 4

Met Lys Lys Thr Leu Arg Asp Gln Leu Leu Gly Val Ser Lys Ala His  
 1 5 10 15

Leu Asn Trp Lys Asn Lys Thr Lys Val Phe Ile Tyr Gly Thr Ala Ile  
 20 25 30

Leu Leu Met Val Ala Pro Asn Leu Ala Ser Ser Val Ser Arg Ala Ser  
 35 40 45

Ala Asp Glu Glu Gly Asn Ala Pro Lys Val Thr Gln Ala Gly Glu Arg  
 50 55 60

Ser Gly Lys Leu Ala Leu Asn Ile Ser His Ser Ala Leu Asp Gln Ala  
 65 70 75 80

Ile Ser Asp Ala Lys Ala Ala Gly Leu Ser Leu Lys Glu Gly Ala Ile  
 85 90 95

-continued

---

Gln Asp Lys Gly Asn Ala Gln Gly Thr Asp Ala Ile Thr Lys Leu Gln  
 100 105 110  
 Lys Ala Ile Ser Asp Asp Tyr Ala Ser Gln Val Ser Thr Ile Lys Lys  
 115 120 125  
 Gln Thr Ser Asp Tyr Lys Thr Ala Leu Asp Ala Tyr Asn Lys Ala Glu  
 130 135 140  
 Ala Asp Tyr Lys Lys Gln Leu Asp Asp Ile Gln Asn Gly Ile Asp Asn  
 145 150 155 160  
 Asn Thr Pro Gly Ser Pro Ala Val Ala Lys Gly Gln Gly Leu Thr Phe  
 165 170 175  
 Arg Ala Gly Gln Asn Pro Lys Ala Thr Val Glu Ser Val Lys Phe Ser  
 180 185 190  
 Gly Ser Gly Asp Gly Ala Leu Leu Lys Ser Lys Val Leu Gly Asp Gly  
 195 200 205  
 Met Thr Gly Leu Ser Lys Val Thr Ser Ser Asp Val Val Ser Gln Pro  
 210 215 220  
 Asp Phe Tyr Asp Leu Gly Gly Thr Thr Ser Leu Phe Gly Leu Phe Leu  
 225 230 235 240  
 Asp Ala Gly Gln Ser Val Thr Ile Thr Tyr Lys Asp Leu Lys Asn Phe  
 245 250 255  
 Ser Leu Asn Gly Thr Ser Val Ile Gln Met Lys Val Thr Tyr Lys Asn  
 260 265 270  
 Val Thr Asn Ala Arg Met Gly Ile Met Val Ser Arg Asp Pro Gly Asn  
 275 280 285  
 Gln Phe Gln Phe Gly Val Glu Thr Asn Gly Arg Ile Phe Val Asn Gln  
 290 295 300  
 Pro Lys Ala Leu Gln Glu Ser Leu Glu Phe His Asp Gly Ser Asn Lys  
 305 310 315 320  
 Leu Met Thr Phe Lys Thr Val Asp Ser Ser Ser Ala Gln Phe Met Ala  
 325 330 335  
 Gly Ser Leu Asn Tyr Ser Lys Ser Lys Thr Pro Glu Gly Gly Leu Pro  
 340 345 350  
 Pro Thr Ser Asp Gly Tyr Asn Gln His Glu Ser Val Ser Phe Asp Asn  
 355 360 365  
 Thr Leu Val Val Gly Ser Tyr Phe Pro Ser Ser Gly Val His Lys Val  
 370 375 380  
 Ser Gly Arg Pro Thr Ser Gly Ala Asn Ala Thr Gly Asp Ser Trp Ser  
 385 390 395 400  
 Ser Asn Pro Pro Ser Thr Asn Glu Thr Trp Ser Ala Thr Ala Tyr Ile  
 405 410 415  
 Asp Tyr Lys Ala Ile Gly Pro Ser Leu Asp Val Thr Glu Trp Asp Val  
 420 425 430  
 Gly Thr Lys Asn Ser Trp Tyr Gly Ala Met Asn Leu Ile Pro Lys Asp  
 435 440 445  
 Gly Gln Thr Ser Ile Ser Val Thr Trp Gly Thr Thr Asp Ala Asn Met  
 450 455 460  
 Trp Ala Leu Leu Asn Gly Gln Leu Pro Asn Lys Ile Pro Thr Pro Glu  
 465 470 475 480  
 Pro Pro Ile Pro Pro Val Lys Pro Thr Ala Thr Tyr Tyr Tyr Asp Gln  
 485 490 495  
 Ala Thr Phe Gln Thr Asp Asn Thr Lys Ala Val Thr Gln Thr Asp Gly  
 500 505 510  
 Thr Asp Leu Asn Gly Ala Leu Val Asn Lys Gln Glu Thr Glu Asn Trp  
 515 520 525

-continued

---

Val Leu Ser Asn Glu Val Leu Pro Ala Gly His Glu Val Ile Lys Ser  
 530 535 540

Tyr Val Met Thr Asp Pro Leu Pro Glu Gly Phe Lys Leu Asp Leu Glu  
 545 550 555 560

Gln Ser Lys Thr Leu Ser Pro Asp Tyr Asp Leu Thr Phe Asp Glu Lys  
 565 570 575

Thr Asn Thr Val Thr Leu Thr Ala Tyr Lys Ala Thr Leu Glu Ala Met  
 580 585 590

Asn Lys Asp Leu Asn Gln Ala Tyr Gln Val Pro Lys Glu Thr Leu Gln  
 595 600 605

Gly Gln Val Thr Lys Asp Gly Ser Ser Phe Lys Asn Asp Leu Glu Thr  
 610 615 620

Leu Ile Asn Asp Tyr Thr Val Asn Ser Asn Glu Val Glu Val His Thr  
 625 630 635 640

Pro Asp Pro Lys Pro Glu Lys Ser Asn Glu Asn Ala Ser Gly Thr Thr  
 645 650 655

Ile Asn Gly Gln Gly Ile Asp Val Asn Ala Thr Asn Tyr Tyr Lys Leu  
 660 665 670

Leu Trp Asp Leu Ser Gly Tyr Lys Gly Ile Ala Ser Ser Lys Glu Asp  
 675 680 685

Ile Val Arg Gly Phe Tyr Phe Val Asp Ala Ala Pro Asp Val Val Asp  
 690 695 700

Val Asp Leu Lys Asn Ile Ser Tyr Lys Asp Ser Gln Gly Lys Glu Val  
 705 710 715 720

Lys Gly Ile Thr Ala Lys Val Tyr Ser Ser Val Lys Asp Ala Pro Ala  
 725 730 735

Glu Val Gln Lys Val Leu Ala Asp Ala Lys Ile Ala Pro Lys Gly Gln  
 740 745 750

Phe Val Phe Tyr Ser Val Asp Asp Pro Gln Thr Phe Tyr Thr Asn Tyr  
 755 760 765

Val Gln Thr Gly Asn Asn Val Glu Ile Thr Gln Pro Met Thr Phe Lys  
 770 775 780

Glu Gly Ala Ser Gly Ala Tyr Gln Asn Thr Asp Tyr Gln Ile Asp Phe  
 785 790 795 800

Gly Asn Ser Tyr Glu Gly Asp Thr Val Lys Asn Asn Ile Val Pro Pro  
 805 810 815

Lys Val Val Lys Gln Val Ser Val Asp Gly Gly Lys Thr Trp His Asp  
 820 825 830

Ser Lys Asp Leu Pro Asp Thr Asp Ser Asn Tyr Asp Tyr Lys Leu Asp  
 835 840 845

Phe Asn Phe Thr Ala Asn Gly Asp Tyr Thr Lys Ile Leu Leu Gly Asp  
 850 855 860

Asn Phe Glu Ser Ser Gln Trp Thr Asp Leu Ala Lys Ala Lys Val Thr  
 865 870 875 880

Asp Lys Asp Gly Asn Asp Ile Ala Gly Gln Phe Lys Val Leu Asn Ala  
 885 890 895

Ser Gly Lys Asp Val Thr Lys Asp Phe Asn Asn His Val Phe Gln Lys  
 900 905 910

Asp Gly Lys Lys Glu Val Leu Gln Ile Ile Phe Thr Pro Asp Lys Ile  
 915 920 925

Ser Asp Ile Thr Ser Leu Ala Ser Asn Ser Asp Pro Asp Arg Leu Ile  
 930 935 940

Thr Leu Thr Met Ser Phe Lys Asp Val Thr Leu Lys Gly Ala Thr Gly

-continued

945	950	955	960
Ala Glu Leu Ala Asn Tyr Leu Asp Lys Glu Gly Lys Ile Val Ala Pro	965	970	975
Asn Ile Gly Gln Leu Asp Thr Thr Ser Arg Thr Val Thr Gly Asp Asn	980	985	990
Thr Lys Asp Lys Ile Thr Lys Ser Asn Val Thr Lys Val Ile Pro Pro	995	1000	1005
Gln Leu Thr Pro Met Ile Asn Lys Tyr Val Tyr Glu Thr Gly Val Gly	1010	1015	1020
Ser Ser Ile Asn Leu Tyr Asp Lys Gly Leu Thr Leu Pro Ser Tyr Leu	1025	1030	1035
Ser Lys Leu Ala Gln Phe Thr Ser Leu Asn Leu Asn Lys Asp Glu Lys	1045	1050	1055
Val Lys Val Gly Glu Thr Val His Trp Leu Ile Ala Thr Gln Ser Gly	1060	1065	1070
Asn Lys Ser Leu Met Thr Asn Val Val Asp Thr Leu Pro Lys Glu Leu	1075	1080	1085
Ser Phe Ala Glu Asn Met Asn Ala Lys Val Phe Val Leu Lys Asn Asp	1090	1095	1100
Gly Lys Leu Gly Asp Glu Val Thr Asn Asp Trp Lys Ile Glu Asn Lys	1105	1110	1115
Gly Gln Thr Leu Thr Ala Thr Pro Asn Asp Pro Thr Lys Tyr Phe Phe	1125	1130	1135
Val Gly Ser Ser Thr Asp Ser Arg Val Val Ile Thr Leu Asp Thr Thr	1140	1145	1150
Val Asn Glu Glu Ala Lys Thr Gly Thr Phe Thr Asn Ile Ala Thr Ile	1155	1160	1165
Asn Thr Lys Asp Gly Gly His Lys Glu Asp Lys Ala Asn Val His Thr	1170	1175	1180
Lys Glu Lys Pro Glu Thr Val Ile Glu Lys Ile Thr Gly Ser Leu Pro	1185	1190	1195
Lys Thr Gly Glu Gly Lys Ala Ala Leu Ala Ile Ser Ile Phe Gly Ala	1205	1210	1215
Ala Leu Leu Gly Leu Ala Ala Tyr Leu Lys Arg Asn Trp Ile Val Ser	1220	1225	1230
Thr Tyr Arg Lys Thr Val Arg Lys Ile Arg Lys	1235	1240	

&lt;210&gt; SEQ ID NO 5

&lt;211&gt; LENGTH: 1575

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Streptococcus gordonii

&lt;400&gt; SEQUENCE: 5

Met Asn Lys Arg Lys Glu Val Phe Gly Phe Arg Lys Ser Lys Val Ala	1	5	10	15
Lys Thr Leu Cys Gly Ala Val Leu Gly Ala Ala Leu Ile Ala Ile Ala	20	25	30	
Asp Gln Gln Val Leu Ala Asp Glu Val Thr Glu Thr Asn Ser Thr Ala	35	40	45	
Asn Val Ala Val Thr Thr Thr Gly Asn Pro Ala Thr Asn Leu Pro Glu	50	55	60	
Ala Gln Gly Glu Ala Thr Glu Ala Ala Ser Gln Ser Gln Ala Gln Ala	65	70	75	80
Gly Ser Lys Glu Gly Ala Leu Pro Val Glu Val Ser Ala Asp Asp Leu				

-continued

85					90					95					
Asn	Gln	Ala	Val	Thr	Asp	Ala	Lys	Ala	Ala	Gly	Val	Asn	Val	Val	Gln
			100					105					110		
Asp	Gln	Thr	Ser	Asp	Lys	Gly	Thr	Ala	Thr	Thr	Ala	Ala	Glu	Asn	Ala
		115					120					125			
Gln	Lys	Gln	Ala	Glu	Ile	Lys	Ser	Asp	Tyr	Ala	Lys	Gln	Ala	Glu	Glu
	130					135					140				
Ile	Lys	Lys	Thr	Thr	Glu	Ala	Tyr	Lys	Lys	Glu	Val	Glu	Ala	His	Gln
145					150					155					160
Ala	Glu	Thr	Asp	Lys	Ile	Asn	Ala	Glu	Asn	Lys	Ala	Ala	Glu	Asp	Lys
				165					170					175	
Tyr	Gln	Glu	Asp	Leu	Lys	Ala	His	Gln	Ala	Glu	Val	Glu	Lys	Ile	Asn
			180					185					190		
Thr	Ala	Asn	Ala	Thr	Ala	Lys	Ala	Glu	Tyr	Glu	Ala	Lys	Leu	Ala	Gln
		195					200					205			
Tyr	Gln	Lys	Asp	Leu	Ala	Ala	Val	Gln	Lys	Ala	Asn	Glu	Asp	Ser	Gln
	210					215					220				
Leu	Asp	Tyr	Gln	Asn	Lys	Leu	Ser	Ala	Tyr	Gln	Ala	Glu	Leu	Ala	Arg
225				230						235					240
Val	Gln	Lys	Ala	Asn	Ala	Glu	Ala	Lys	Glu	Ala	Tyr	Glu	Lys	Ala	Val
				245					250					255	
Lys	Glu	Asn	Thr	Ala	Lys	Asn	Ala	Ala	Leu	Gln	Ala	Glu	Asn	Glu	Ala
			260					265					270		
Ile	Lys	Gln	Arg	Asn	Glu	Thr	Ala	Lys	Ala	Asn	Tyr	Asp	Ala	Ala	Met
		275					280					285			
Lys	Gln	Tyr	Glu	Ala	Asp	Leu	Ala	Ala	Ile	Lys	Lys	Ala	Lys	Glu	Asp
	290					295					300				
Asn	Asp	Ala	Asp	Tyr	Gln	Ala	Lys	Leu	Ala	Ala	Tyr	Gln	Ala	Glu	Leu
305					310					315					320
Ala	Arg	Val	Gln	Lys	Ala	Asn	Ala	Asp	Ala	Lys	Ala	Ala	Tyr	Glu	Lys
				325					330					335	
Ala	Val	Glu	Glu	Asn	Thr	Ala	Lys	Asn	Thr	Ala	Ile	Gln	Ala	Glu	Asn
				340				345					350		
Glu	Ala	Ile	Lys	Gln	Arg	Asn	Ala	Ala	Ala	Lys	Ala	Thr	Tyr	Glu	Ala
		355					360					365			
Ala	Leu	Lys	Gln	Tyr	Glu	Ala	Asp	Leu	Ala	Ala	Ala	Lys	Lys	Ala	Asn
370						375					380				
Glu	Asp	Ser	Asp	Ala	Asp	Tyr	Gln	Ala	Lys	Leu	Ala	Ala	Tyr	Gln	Thr
385						390					395				400
Glu	Leu	Ala	Arg	Val	Gln	Lys	Ala	Asn	Ala	Asp	Ala	Lys	Ala	Ala	Tyr
				405					410					415	
Glu	Lys	Ala	Val	Glu	Asp	Asn	Lys	Ala	Lys	Asn	Ala	Ala	Leu	Gln	Ala
			420					425					430		
Glu	Asn	Glu	Glu	Ile	Lys	Gln	Arg	Asn	Ala	Ala	Ala	Lys	Thr	Asp	Tyr
		435					440					445			
Glu	Ala	Lys	Leu	Ala	Lys	Tyr	Glu	Ala	Asp	Leu	Ala	Lys	Tyr	Lys	Lys
		450				455					460				
Glu	Leu	Ala	Glu	Tyr	Pro	Ala	Lys	Leu	Lys	Ala	Tyr	Glu	Asp	Glu	Gln
465						470					475				480
Ala	Gln	Ile	Lys	Ala	Ala	Leu	Val	Glu	Leu	Glu	Lys	Asn	Lys	Asn	Gln
			485						490					495	
Asp	Gly	Tyr	Leu	Ser	Lys	Pro	Ser	Ala	Gln	Ser	Leu	Val	Tyr	Asp	Ser
			500					505					510		

-continued

Glu	Pro	Asn	Ala	Gln	Leu	Ser	Leu	Thr	Thr	Asn	Gly	Lys	Met	Leu	Lys
		515					520					525			
Ala	Ser	Ala	Val	Asp	Glu	Ala	Phe	Ser	His	Asp	Thr	Ala	Gln	Tyr	Ser
		530				535					540				
Lys	Lys	Ile	Leu	Gln	Pro	Asp	Asn	Leu	Asn	Val	Ser	Tyr	Leu	Gln	Gln
545					550					555					560
Ala	Asp	Asp	Val	Thr	Ser	Ser	Met	Glu	Leu	Tyr	Gly	Asn	Phe	Gly	Asp
				565					570					575	
Lys	Ala	Gly	Trp	Thr	Thr	Thr	Val	Gly	Asn	Asn	Thr	Glu	Val	Lys	Phe
			580					585					590		
Ala	Ser	Val	Leu	Leu	Glu	Arg	Gly	Gln	Ser	Val	Thr	Ala	Thr	Tyr	Thr
		595					600					605			
Asn	Leu	Glu	Lys	Ser	Tyr	Tyr	Asn	Gly	Lys	Lys	Ile	Ser	Lys	Ala	Val
	610					615					620				
Phe	Lys	Tyr	Ser	Leu	Asp	Ser	Asp	Ser	Lys	Phe	Lys	Asn	Val	Asp	Lys
625					630					635					640
Ala	Trp	Leu	Gly	Val	Leu	Pro	Asp	Pro	Thr	Leu	Gly	Val	Phe	Ala	Ser
				645					650					655	
Ala	Tyr	Thr	Gly	Gln	Glu	Glu	Lys	Asp	Thr	Ser	Ile	Phe	Ile	Lys	Asn
			660					665					670		
Glu	Phe	Thr	Phe	Tyr	Asp	Glu	Asn	Asp	Gln	Pro	Ile	Asn	Phe	Asp	Asn
		675					680						685		
Ala	Leu	Leu	Ser	Val	Ala	Ser	Leu	Asn	Arg	Glu	Asn	Asn	Ser	Ile	Glu
	690					695					700				
Met	Ala	Lys	Asp	Tyr	Ser	Gly	Thr	Phe	Val	Lys	Ile	Ser	Gly	Ser	Ser
705					710					715					720
Val	Gly	Glu	Lys	Asp	Gly	Lys	Ile	Tyr	Ala	Thr	Glu	Thr	Leu	Asn	Phe
				725					730					735	
Lys	Gln	Gly	Gln	Gly	Gly	Ser	Arg	Trp	Thr	Met	Tyr	Lys	Asn	Ser	Gln
			740					745					750		
Pro	Gly	Ser	Gly	Trp	Asp	Ser	Ser	Asp	Ala	Pro	Asn	Ser	Trp	Tyr	Gly
		755					760					765			
Ala	Gly	Ala	Ile	Ser	Met	Ser	Gly	Pro	Thr	Asn	His	Val	Thr	Val	Gly
	770					775					780				
Ala	Ile	Ser	Ala	Thr	Gln	Val	Val	Pro	Ser	Asp	Pro	Val	Met	Ala	Val
785					790					795					800
Ala	Thr	Gly	Lys	Arg	Pro	Asn	Ile	Trp	Tyr	Ser	Leu	Asn	Gly	Lys	Ile
				805					810					815	
Arg	Ala	Val	Asn	Val	Pro	Lys	Ile	Thr	Lys	Glu	Lys	Pro	Thr	Pro	Pro
			820						825					830	
Val	Ala	Pro	Thr	Glu	Pro	Gln	Ala	Pro	Thr	Tyr	Glu	Val	Glu	Lys	Pro
		835					840					845			
Leu	Glu	Pro	Ala	Pro	Val	Ala	Pro	Thr	Tyr	Glu	Asn	Glu	Pro	Thr	Pro
	850					855					860				
Pro	Val	Lys	Thr	Pro	Asp	Gln	Pro	Glu	Pro	Ser	Lys	Pro	Glu	Glu	Pro
865					870					875					880
Thr	Tyr	Glu	Thr	Glu	Lys	Pro	Leu	Glu	Pro	Ala	Pro	Val	Val	Pro	Thr
				885					890					895	
Tyr	Glu	Asn	Glu	Pro	Thr	Pro	Pro	Val	Lys	Thr	Pro	Asp	Gln	Pro	Glu
			900					905					910		
Pro	Ser	Lys	Pro	Glu	Glu	Pro	Thr	Tyr	Glu	Thr	Glu	Lys	Pro	Leu	Glu
		915					920					925			
Pro	Ala	Pro	Val	Ala	Pro	Thr	Tyr	Glu	Asn	Glu	Pro	Thr	Pro	Pro	Val
						935						940			



-continued

---

Lys Thr Pro Asp Gln Pro Glu Pro Ser Lys Pro Glu Glu Pro Thr Tyr  
 945 950 955 960  
 Asp Pro Leu Pro Thr Pro Pro Val Ala Pro Thr Pro Lys Gln Leu Pro  
 965 970 975  
 Thr Pro Pro Val Val Pro Thr Val His Phe His Tyr Ser Ser Leu Leu  
 980 985 990  
 Ala Gln Pro Gln Ile Asn Lys Glu Ile Lys Asn Glu Asp Gly Val Asp  
 995 1000 1005  
 Ile Asp Arg Thr Leu Val Ala Lys Gln Ser Ile Val Lys Phe Glu Leu  
 1010 1015 1020  
 Lys Thr Glu Ala Leu Thr Ala Gly Arg Pro Lys Thr Thr Ser Phe Val  
 1025 1030 1035 1040  
 Leu Val Asp Pro Leu Pro Thr Gly Tyr Lys Phe Asp Leu Asp Ala Thr  
 1045 1050 1055  
 Lys Ala Ala Ser Thr Gly Phe Asp Thr Thr Tyr Asp Glu Ala Ser His  
 1060 1065 1070  
 Thr Val Thr Phe Lys Ala Thr Asp Glu Thr Leu Ala Thr Tyr Asn Ala  
 1075 1080 1085  
 Asp Leu Thr Lys Pro Val Glu Thr Leu His Pro Thr Val Val Gly Arg  
 1090 1095 1100  
 Val Leu Asn Asp Gly Ala Thr Tyr Ile Asn Asn Phe Thr Leu Thr Val  
 1105 1110 1115 1120  
 Asn Asp Ala Tyr Gly Ile Lys Ser Asn Val Val Arg Val Thr Thr Pro  
 1125 1130 1135  
 Gly Lys Pro Asn Asp Pro Asp Asn Pro Asn Asn Asn Tyr Ile Lys Pro  
 1140 1145 1150  
 Thr Lys Val Asn Lys Asn Lys Glu Gly Leu Asn Ile Asp Gly Lys Glu  
 1155 1160 1165  
 Val Leu Ala Gly Ser Thr Asn Tyr Tyr Glu Leu Thr Trp Asp Leu Asp  
 1170 1175 1180  
 Gln Tyr Lys Gly Asp Lys Ser Ser Lys Glu Ala Ile Gln Asn Gly Phe  
 1185 1190 1195 1200  
 Tyr Tyr Val Asp Asp Tyr Pro Glu Glu Ala Leu Asp Val Arg Pro Asp  
 1205 1210 1215  
 Leu Val Lys Val Ala Asp Glu Lys Gly Asn Gln Val Ser Gly Val Ser  
 1220 1225 1230  
 Val Gln Gln Tyr Asp Ser Leu Glu Ala Ala Pro Lys Lys Val Gln Asp  
 1235 1240 1245  
 Leu Leu Lys Lys Ala Asn Ile Thr Val Lys Gly Ala Phe Gln Leu Phe  
 1250 1255 1260  
 Ser Ala Asp Asn Pro Glu Glu Phe Tyr Lys Gln Tyr Val Ser Thr Gly  
 1265 1270 1275 1280  
 Thr Ser Leu Val Ile Thr Asp Pro Met Thr Val Lys Ser Glu Phe Gly  
 1285 1290 1295  
 Lys Thr Gly Gly Lys Tyr Glu Asn Lys Ala Tyr Gln Ile Asp Phe Gly  
 1300 1305 1310  
 Asn Gly Tyr Ala Thr Glu Val Val Val Asn Asn Val Pro Lys Ile Thr  
 1315 1320 1325  
 Pro Lys Lys Asp Val Thr Val Ser Leu Asp Pro Thr Ser Glu Asn Leu  
 1330 1335 1340  
 Asp Gly Gln Thr Val Gln Leu Tyr Gln Thr Phe Asn Tyr Arg Leu Ile  
 1345 1350 1355 1360  
 Gly Gly Phe Ile Pro Gln Asn His Ser Glu Glu Leu Glu Asp Tyr Ser

-continued

1365	1370	1375
Phe Val Asp Asp Tyr Asp Gln Ala Gly Asp Gln Tyr Thr Gly Asn Tyr 1380 1385 1390		
Lys Thr Phe Ser Ser Leu Asn Leu Thr Met Lys Asp Gly Ser Val Ile 1395 1400 1405		
Lys Ala Gly Thr Asp Leu Thr Ser Gln Thr Thr Ala Glu Thr Asp Ala 1410 1415 1420		
Ala Asn Gly Ile Val Thr Val Arg Ser Lys Glu Asp Ser Leu Gln Lys 1425 1430 1435 1440		
Ile Ser Leu Asp Ser Pro Phe Gln Ala Glu Thr Tyr Leu Gln Met Arg 1445 1450 1455		
Arg Ile Ala Ile Gly Thr Phe Glu Asn Thr Tyr Val Asn Thr Val Asn 1460 1465 1470		
Lys Val Ala Tyr Ala Ser Asn Thr Val Arg Thr Thr Thr Pro Ile Pro 1475 1480 1485		
Arg Thr Pro Asp Lys Pro Thr Pro Ile Pro Thr Pro Lys Pro Lys Asp 1490 1495 1500		
Pro Asp Lys Pro Glu Thr Pro Lys Glu Pro Lys Val Pro Ser Pro Lys 1505 1510 1515 1520		
Val Glu Asp Pro Ser Ala Pro Ile Pro Val Ser Val Gly Lys Glu Leu 1525 1530 1535		
Thr Thr Leu Pro Lys Thr Gly Thr Asn Asp Ser Ser Tyr Met Pro Tyr 1540 1545 1550		
Leu Gly Leu Ala Ala Leu Val Gly Val Leu Gly Leu Gly Gln Leu Lys 1555 1560 1565		
Arg Lys Glu Asp Glu Ser Asn 1570 1575		

&lt;210&gt; SEQ ID NO 6

&lt;211&gt; LENGTH: 1565

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Streptococcus mutans

&lt;400&gt; SEQUENCE: 6

Met Lys Val Lys Lys Thr Tyr Gly Phe Arg Lys Ser Lys Ile Ser Lys 1 5 10 15
Thr Leu Cys Gly Ala Val Leu Gly Thr Val Ala Ala Val Ser Val Ala 20 25 30
Gly Gln Lys Val Phe Ala Asp Glu Thr Thr Thr Thr Ser Asp Val Asp 35 40 45
Thr Lys Val Val Gly Thr Gln Thr Gly Asn Pro Ala Thr Asn Leu Pro 50 55 60
Glu Ala Gln Gly Ser Ala Ser Lys Glu Ala Glu Gln Ser Gln Thr Lys 65 70 75 80
Leu Glu Arg Gln Met Val His Thr Ile Glu Val Pro Lys Thr Asp Leu 85 90 95
Asp Gln Ala Ala Lys Asp Ala Lys Ser Ala Gly Val Asn Val Val Gln 100 105 110
Asp Ala Asp Val Asn Lys Gly Thr Val Lys Thr Pro Glu Glu Ala Val 115 120 125
Gln Lys Glu Thr Glu Ile Lys Glu Asp Tyr Thr Lys Gln Ala Glu Asp 130 135 140
Ile Lys Lys Thr Thr Asp Gln Tyr Lys Ser Asp Val Ala Ala His Glu 145 150 155 160
Ala Glu Val Ala Lys Ile Lys Ala Lys Asn Gln Ala Thr Lys Glu Gln

-continued

165					170					175					
Tyr	Glu	Lys	Asp	Met	Ala	Ala	His	Lys	Ala	Glu	Val	Glu	Arg	Ile	Asn
			180					185					190		
Ala	Ala	Asn	Ala	Ala	Ser	Lys	Thr	Ala	Tyr	Glu	Ala	Lys	Leu	Ala	Gln
		195					200					205			
Tyr	Gln	Ala	Asp	Leu	Ala	Ala	Val	Gln	Lys	Thr	Asn	Ala	Ala	Asn	Gln
	210					215					220				
Ala	Ala	Tyr	Gln	Lys	Ala	Leu	Ala	Ala	Tyr	Gln	Ala	Glu	Leu	Lys	Arg
225						230					235				240
Val	Gln	Glu	Ala	Asn	Ala	Ala	Ala	Lys	Ala	Ala	Tyr	Asp	Thr	Ala	Val
			245						250					255	
Ala	Ala	Asn	Asn	Ala	Lys	Asn	Thr	Glu	Ile	Ala	Ala	Ala	Asn	Glu	Glu
		260						265						270	
Ile	Arg	Lys	Arg	Asn	Ala	Thr	Ala	Lys	Ala	Glu	Tyr	Glu	Thr	Lys	Leu
		275					280						285		
Ala	Gln	Tyr	Gln	Ala	Glu	Leu	Lys	Arg	Val	Gln	Glu	Ala	Asn	Ala	Ala
	290					295					300				
Asn	Glu	Ala	Asp	Tyr	Gln	Ala	Lys	Leu	Thr	Ala	Tyr	Gln	Thr	Glu	Leu
305				310							315				320
Ala	Arg	Val	Gln	Lys	Ala	Asn	Ala	Asp	Ala	Lys	Ala	Thr	Tyr	Glu	Ala
			325						330					335	
Ala	Val	Ala	Ala	Asn	Asn	Ala	Lys	Asn	Ala	Ala	Leu	Thr	Ala	Glu	Asn
		340						345						350	
Thr	Ala	Ile	Lys	Gln	Arg	Asn	Glu	Asn	Ala	Lys	Ala	Thr	Tyr	Glu	Ala
		355					360						365		
Ala	Leu	Lys	Gln	Tyr	Glu	Ala	Asp	Leu	Ala	Ala	Val	Lys	Lys	Ala	Asn
	370					375					380				
Ala	Ala	Asn	Glu	Ala	Asp	Tyr	Gln	Ala	Lys	Leu	Thr	Ala	Tyr	Gln	Thr
385				390							395				400
Glu	Leu	Ala	Arg	Val	Gln	Lys	Ala	Asn	Ala	Asp	Ala	Lys	Ala	Ala	Tyr
			405						410					415	
Glu	Ala	Ala	Val	Ala	Ala	Asn	Asn	Ala	Ala	Asn	Ala	Ala	Leu	Thr	Ala
			420					425						430	
Glu	Asn	Thr	Ala	Ile	Lys	Lys	Arg	Asn	Ala	Asp	Ala	Lys	Ala	Asp	Tyr
		435					440					445			
Glu	Ala	Lys	Leu	Ala	Lys	Tyr	Gln	Ala	Asp	Leu	Ala	Lys	Tyr	Gln	Lys
	450					455					460				
Asp	Leu	Ala	Asp	Tyr	Pro	Val	Lys	Leu	Lys	Ala	Tyr	Glu	Asp	Glu	Gln
465				470							475				480
Thr	Ser	Ile	Lys	Ala	Ala	Leu	Ala	Glu	Leu	Glu	Lys	His	Lys	Asn	Glu
			485						490					495	
Asp	Gly	Asn	Leu	Thr	Glu	Pro	Ser	Ala	Gln	Asn	Leu	Val	Tyr	Asp	Leu
		500						505					510		
Glu	Pro	Asn	Ala	Asn	Leu	Ser	Leu	Thr	Thr	Asp	Gly	Lys	Phe	Leu	Lys
		515					520					525			
Ala	Ser	Ala	Val	Asp	Asp	Ala	Phe	Ser	Lys	Ser	Thr	Ser	Lys	Ala	Lys
	530					535					540				
Tyr	Asp	Gln	Lys	Ile	Leu	Gln	Leu	Asp	Asp	Leu	Asp	Ile	Thr	Asn	Leu
545				550							555				560
Glu	Gln	Ser	Asn	Asp	Val	Ala	Ser	Ser	Met	Glu	Leu	Tyr	Gly	Asn	Phe
			565						570					575	
Gly	Asp	Lys	Ala	Gly	Trp	Ser	Thr	Thr	Val	Ser	Asn	Asn	Ser	Gln	Val
		580						585					590		

-continued

Lys	Trp	Gly	Ser	Val	Leu	Leu	Glu	Arg	Gly	Gln	Ser	Ala	Thr	Ala	Thr
		595					600					605			
Tyr	Thr	Asn	Leu	Gln	Asn	Ser	Tyr	Tyr	Asn	Gly	Lys	Lys	Ile	Ser	Lys
		610				615					620				
Ile	Val	Tyr	Lys	Tyr	Thr	Val	Asp	Pro	Lys	Ser	Lys	Phe	Gln	Gly	Gln
625					630					635					640
Lys	Val	Trp	Leu	Gly	Ile	Phe	Thr	Asp	Pro	Thr	Leu	Gly	Val	Phe	Ala
				645					650					655	
Ser	Ala	Tyr	Thr	Gly	Gln	Val	Glu	Lys	Asn	Thr	Ser	Ile	Phe	Ile	Lys
			660					665					670		
Asn	Glu	Phe	Thr	Phe	Tyr	His	Glu	Asp	Glu	Lys	Pro	Ile	Asn	Phe	Asp
		675					680					685			
Asn	Ala	Leu	Leu	Ser	Val	Thr	Ser	Leu	Asn	Arg	Glu	His	Asn	Ser	Ile
		690				695					700				
Glu	Met	Ala	Lys	Asp	Tyr	Ser	Gly	Lys	Phe	Val	Lys	Ile	Ser	Gly	Ser
705					710					715					720
Ser	Ile	Gly	Glu	Lys	Asn	Gly	Met	Ile	Tyr	Ala	Thr	Asp	Thr	Leu	Asn
				725					730					735	
Phe	Lys	Gln	Gly	Glu	Gly	Gly	Ser	Arg	Trp	Thr	Met	Tyr	Lys	Asn	Ser
			740					745					750		
Gln	Ala	Gly	Ser	Gly	Trp	Asp	Ser	Ser	Asp	Ala	Pro	Asn	Ser	Trp	Tyr
		755					760					765			
Gly	Ala	Gly	Ala	Ile	Lys	Met	Ser	Gly	Pro	Asn	Asn	His	Val	Thr	Val
		770				775					780				
Gly	Ala	Thr	Ser	Ala	Thr	Asn	Val	Met	Pro	Val	Ser	Asp	Met	Pro	Val
785					790					795					800
Val	Pro	Gly	Lys	Asp	Asn	Thr	Asp	Gly	Lys	Lys	Pro	Asn	Ile	Trp	Tyr
				805					810					815	
Ser	Leu	Asn	Gly	Lys	Ile	Arg	Ala	Val	Asn	Val	Pro	Lys	Val	Thr	Lys
			820					825					830		
Glu	Lys	Pro	Thr	Pro	Pro	Val	Lys	Pro	Thr	Ala	Pro	Thr	Lys	Pro	Thr
		835					840					845			
Tyr	Glu	Thr	Glu	Lys	Pro	Leu	Lys	Pro	Ala	Pro	Val	Ala	Pro	Asn	Tyr
		850				855					860				
Glu	Lys	Glu	Pro	Thr	Pro	Pro	Thr	Arg	Thr	Pro	Asp	Gln	Ala	Glu	Pro
865					870					875					880
Asn	Lys	Pro	Thr	Pro	Pro	Thr	Tyr	Glu	Thr	Glu	Lys	Pro	Leu	Glu	Pro
				885					890					895	
Ala	Pro	Val	Glu	Pro	Ser	Tyr	Glu	Ala	Glu	Pro	Thr	Pro	Pro	Thr	Arg
			900					905					910		
Thr	Pro	Asp	Gln	Ala	Glu	Pro	Asn	Lys	Pro	Thr	Pro	Pro	Thr	Tyr	Glu
		915					920					925			
Thr	Glu	Lys	Pro	Leu	Glu	Pro	Ala	Pro	Val	Glu	Pro	Ser	Tyr	Glu	Ala
		930				935					940				
Glu	Pro	Thr	Pro	Pro	Thr	Pro	Thr	Pro	Asp	Gln	Pro	Glu	Pro	Asn	Lys
945					950					955					960
Pro	Val	Glu	Pro	Thr	Tyr	Glu	Val	Ile	Pro	Thr	Pro	Pro	Thr	Asp	Pro
				965					970					975	
Val	Tyr	Gln	Asp	Leu	Pro	Thr	Pro	Pro	Ser	Asp	Pro	Thr	Val	His	Phe
			980					985					990		
His	Tyr	Phe	Lys	Leu	Ala	Val	Gln	Pro	Gln	Val	Asn	Lys	Glu	Ile	Arg
		995				1000						1005			
Asn	Asn	Asn	Asp	Ile	Asn	Ile	Asp	Arg	Thr	Leu	Val	Ala	Lys	Gln	Ser
1010						1015					1020				

-continued

---

Val Val Lys Phe Gln Leu Lys Thr Ala Asp Leu Pro Ala Gly Arg Asp  
 1025 1030 1035 1040  
 Glu Thr Thr Ser Phe Val Leu Val Asp Pro Leu Pro Ser Gly Tyr Gln  
 1045 1050 1055  
 Phe Asn Pro Glu Ala Thr Lys Ala Ala Ser Pro Gly Phe Asp Val Thr  
 1060 1065 1070  
 Tyr Asp Asn Ala Thr Asn Thr Val Thr Phe Lys Ala Thr Ala Ala Thr  
 1075 1080 1085  
 Leu Ala Thr Phe Asn Ala Asp Leu Thr Lys Ser Val Ala Thr Ile Tyr  
 1090 1095 1100  
 Pro Thr Val Val Gly Gln Val Leu Asn Asp Gly Ala Thr Tyr Lys Asn  
 1105 1110 1115 1120  
 Asn Phe Thr Leu Thr Val Asn Asp Ala Tyr Gly Ile Lys Ser Asn Val  
 1125 1130 1135  
 Val Arg Val Thr Thr Pro Gly Lys Pro Asn Asp Pro Asp Asn Pro Asn  
 1140 1145 1150  
 Asn Asn Tyr Ile Lys Pro Thr Lys Val Asn Lys Asn Glu Asn Gly Val  
 1155 1160 1165  
 Val Ile Asp Gly Lys Thr Val Leu Ala Gly Ser Thr Asn Tyr Tyr Glu  
 1170 1175 1180  
 Leu Thr Trp Asp Leu Asp Gln Tyr Lys Asn Asp Arg Ser Ser Ala Asp  
 1185 1190 1195 1200  
 Thr Ile Gln Lys Gly Phe Tyr Tyr Val Asp Asp Tyr Pro Glu Glu Ala  
 1205 1210 1215  
 Leu Glu Leu Arg Gln Asp Leu Val Lys Ile Thr Asp Ala Asn Gly Asn  
 1220 1225 1230  
 Glu Val Thr Gly Val Ser Val Asp Asn Tyr Thr Asn Leu Glu Ala Ala  
 1235 1240 1245  
 Pro Gln Glu Ile Arg Asp Val Leu Ser Lys Ala Gly Ile Arg Pro Lys  
 1250 1255 1260  
 Gly Ala Phe Gln Ile Phe Arg Ala Asp Asn Pro Arg Glu Phe Tyr Asp  
 1265 1270 1275 1280  
 Thr Tyr Val Lys Thr Gly Ile Asp Leu Lys Ile Val Ser Pro Met Val  
 1285 1290 1295  
 Val Lys Lys Gln Met Gly Gln Thr Gly Gly Ser Tyr Glu Asn Gln Ala  
 1300 1305 1310  
 Tyr Gln Ile Asp Phe Gly Asn Gly Tyr Ala Ser Asn Ile Val Ile Asn  
 1315 1320 1325  
 Asn Val Pro Lys Ile Asn Pro Lys Lys Asp Val Thr Leu Thr Leu Asp  
 1330 1335 1340  
 Pro Ala Asp Thr Asn Asn Val Asp Gly Gln Thr Ile Pro Leu Asn Thr  
 1345 1350 1355 1360  
 Val Phe Asn Tyr Arg Leu Ile Gly Gly Ile Ile Pro Ala Asn His Ser  
 1365 1370 1375  
 Glu Glu Leu Phe Glu Tyr Asn Phe Tyr Asp Asp Tyr Asp Gln Thr Gly  
 1380 1385 1390  
 Asp His Tyr Thr Gly Gln Tyr Lys Val Phe Ala Lys Val Asp Ile Thr  
 1395 1400 1405  
 Leu Lys Asn Gly Val Ile Ile Lys Ser Gly Thr Glu Leu Thr Gln Tyr  
 1410 1415 1420  
 Thr Thr Ala Glu Val Asp Thr Thr Lys Gly Ala Ile Thr Ile Lys Phe  
 1425 1430 1435 1440  
 Lys Glu Ala Phe Leu Arg Ser Val Ser Ile Asp Ser Ala Phe Gln Ala

-continued

1445	1450	1455
Glu Ser Tyr Ile Gln Met Lys Arg Ile Ala Val Gly Thr Phe Glu Asn		
1460	1465	1470
Thr Tyr Ile Asn Thr Val Asn Gly Val Thr Tyr Ser Ser Asn Thr Val		
1475	1480	1485
Lys Thr Thr Thr Pro Glu Asp Pro Ala Asp Pro Thr Asp Pro Gln Asp		
1490	1495	1500
Pro Ser Ser Pro Arg Thr Ser Thr Val Ile Ile Tyr Lys Pro Gln Ser		
1505	1510	1515
Thr Ala Tyr Gln Pro Ser Ser Val Gln Glu Thr Leu Pro Asn Thr Gly		
1525	1530	1535
Val Thr Asn Asn Ala Tyr Met Pro Leu Leu Gly Ile Ile Gly Leu Val		
1540	1545	1550
Thr Ser Phe Ser Leu Leu Gly Leu Lys Ala Lys Lys Asp		
1555	1560	1565

&lt;210&gt; SEQ ID NO 7

&lt;211&gt; LENGTH: 325

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Lactococcus lactis

&lt;400&gt; SEQUENCE: 7

Met Glu Lys Gly Leu Leu Val Asp Ile Gly Arg Lys Tyr Trp Ser Ile			
1	5	10	15
Ala Glu Leu Lys Arg Leu Val Leu Leu Leu Gln Glu His Lys Leu Thr			
20	25	30	
His Leu Gln Leu His Leu Asn Glu Asn Glu Gly Phe Ala Leu Asn Phe			
35	40	45	
Thr Asp Ser Pro Val Ser Lys Lys Tyr Ser Glu Asn Met Leu Lys Glu			
50	55	60	
Leu Lys Glu Phe Ala Lys Thr His Glu Ile Thr Leu Ile Pro Asp Phe			
65	70	75	80
Asp Ser Pro Gly His Met Gly Ser Leu Leu Glu Gln Asn Pro Glu Phe			
85	90	95	
Ala Leu Pro Asp Ser Asn Gln Gln Ala Val Asp Val Thr Asn Pro Ala			
100	105	110	
Val Ile Asp Trp Ile Met Gly Ile Ile Asp Lys Ile Val Asp Ile Phe			
115	120	125	
Pro Asp Ser Asp Thr Phe His Ile Gly Ala Asp Glu Phe Ile Asp Phe			
130	135	140	
Arg Gln Ile Glu Lys Tyr Pro Tyr Leu Val Glu Lys Thr Arg Glu Lys			
145	150	155	160
Tyr Gly Asn Lys Ala Ser Gly Leu Glu Phe Tyr Tyr Asp Tyr Val Asn			
165	170	175	
Gln Leu Thr Glu His Leu Gln Lys Lys Gly Lys Gln Val Arg Ile Trp			
180	185	190	
Asn Asp Gly Phe Leu Arg Lys Asp Leu Gln Ser Leu Val Pro Leu Asn			
195	200	205	
Lys Asn Val Glu Val Cys Tyr Trp Thr Asn Trp Asp Lys Gly Met Ala			
210	215	220	
Glu Val Lys Glu Trp Leu Thr Lys Gly Tyr Thr Leu Ile Asn Phe Cys			
225	230	235	240
Asp Asn Asp Leu Tyr Tyr Val Leu Gly Glu Glu Ala Gly Tyr Ser Tyr			
245	250	255	
Pro Thr Ala Glu Lys Leu Glu Arg Glu Gly Lys Ile Gln Lys Phe Ser			

-continued

260					265					270					
Gly	Gln	Gln	Tyr	Leu	Asn	Gln	Glu	Glu	Met	Lys	Ala	Val	Arg	Gly	Thr
		275					280					285			
Tyr	Phe	Ser	Ile	Trp	Ala	Asp	Asn	Ala	Ala	Ala	Lys	Ser	Val	Ser	Glu
	290					295					300				
Ile	Leu	Asp	Asp	Leu	Ser	Lys	Val	Leu	Pro	Val	Phe	Met	Lys	Ile	Tyr
305						310					315				320
Gly	Gly	Asn	Asp	Glu											
				325											
<210> SEQ ID NO 8															
<211> LENGTH: 355															
<212> TYPE: PRT															
<213> ORGANISM: Lactobacillus johnsonii															
<400> SEQUENCE: 8															
Met	Phe	Val	Lys	Leu	Leu	Arg	Ser	Val	Ala	Ile	Gly	Leu	Ile	Val	Gly
1				5					10					15	
Ala	Ile	Leu	Leu	Val	Ala	Met	Pro	Ser	Leu	Arg	Ser	Leu	Asn	Pro	Leu
			20					25					30		
Ser	Thr	Pro	Gln	Phe	Asp	Ser	Thr	Asp	Glu	Thr	Pro	Ala	Ser	Tyr	Asn
		35					40					45			
Leu	Ala	Val	Arg	Arg	Ala	Ala	Pro	Ala	Val	Val	Asn	Val	Tyr	Asn	Arg
	50					55					60				
Gly	Leu	Asn	Thr	Asn	Ser	His	Asn	Gln	Leu	Glu	Ile	Arg	Thr	Leu	Gly
65				70							75				80
Ser	Gly	Val	Ile	Met	Asp	Gln	Arg	Gly	Tyr	Ile	Ile	Thr	Asn	Lys	His
				85					90					95	
Val	Ile	Asn	Asp	Ala	Asp	Gln	Ile	Ile	Val	Ala	Leu	Gln	Asp	Gly	Arg
			100						105				110		
Val	Phe	Glu	Ala	Leu	Leu	Val	Gly	Ser	Asp	Ser	Leu	Thr	Asp	Leu	Ala
	115						120					125			
Val	Leu	Lys	Ile	Asn	Ala	Thr	Gly	Gly	Leu	Pro	Thr	Ile	Pro	Ile	Asn
	130					135					140				
Ala	Arg	Arg	Val	Pro	His	Ile	Gly	Asp	Val	Val	Leu	Ala	Ile	Gly	Asn
145						150					155				160
Pro	Tyr	Asn	Leu	Gly	Gln	Thr	Ile	Thr	Gln	Gly	Ile	Ile	Ser	Ala	Thr
				165					170					175	
Gly	Arg	Ile	Gly	Leu	Asn	Pro	Thr	Gly	Arg	Gln	Asn	Phe	Leu	Gln	Thr
			180					185					190		
Asp	Ala	Ser	Ile	Asn	His	Gly	Asn	Ser	Gly	Gly	Ala	Leu	Val	Asn	Ser
	195						200					205			
Leu	Gly	Glu	Leu	Met	Gly	Ile	Asn	Thr	Leu	Ser	Phe	Asp	Lys	Ser	Asn
	210					215					220				
Asp	Gly	Glu	Thr	Pro	Glu	Gly	Ile	Gly	Phe	Ala	Ile	Pro	Phe	Gln	Leu
225						230					235				240
Ala	Thr	Lys	Ile	Met	Asp	Lys	Leu	Ile	Arg	Asp	Gly	Arg	Val	Ile	Arg
				245					250					255	
Gly	Tyr	Ile	Gly	Ile	Gly	Gly	Arg	Glu	Ile	Ala	Pro	Leu	His	Ala	Gln
			260					265					270		
Gly	Gly	Gly	Ile	Asp	Gln	Leu	Gln	Gly	Ile	Val	Val	Asn	Glu	Val	Ser
		275					280					285			
Pro	Asp	Gly	Pro	Ala	Ala	Asn	Ala	Gly	Ile	Gln	Val	Asn	Asp	Leu	Ile
	290					295					300				
Ile	Ser	Val	Asp	Asn	Lys	Pro	Ala	Ile	Ser	Ala	Leu	Glu	Thr	Met	Asp

-continued

```

305             310             315             320
Gln Val Ala Glu Ile Arg Pro Gly Ser Val Ile Pro Val Val Val Met
             325             330             335
Arg Asp Asp Lys Gln Leu Thr Leu Gln Val Thr Ile Gln Glu Tyr Pro
             340             345             350
Ala Thr Asn
             355
<210> SEQ ID NO 9
<211> LENGTH: 423
<212> TYPE: PRT
<213> ORGANISM: Lactobacillus acidophilus
<400> SEQUENCE: 9
Met Ile Leu Gly Asn Met Arg Gly Glu Leu Ser Met Val Glu Asn Gln
  1             5             10             15
Asn Asn Asn Gln Arg Pro Arg Lys Asn Ser Asn Ala Lys Ile Ile Thr
           20           25           30
Thr Ala Ala Ile Val Gly Val Val Gly Gly Leu Ile Gly Gly Gly Val
  35           40           45
Ser Tyr Tyr Ala Ala Asp Gln Met Asn Asn Ala Thr Asp Thr Thr Thr
  50           55           60
Ala Gln Thr Ser Val Ser Ser Asn Ser Ser Lys Val Ser Glu Lys Ser
  65           70           75           80
Ala Lys Thr Ser Gly Thr Met Thr Thr Ala Tyr Asn Asp Val Lys Gly
           85           90           95
Ala Val Val Ser Val Ile Asn Leu Lys Arg Gln Ser Ser Ser Ser Ser
           100          105          110
Ala Asn Ser Leu Tyr Ser Ser Leu Phe Gly Asp Asp Ser Asp Ser Ser
           115          120          125
Ser Gly Lys Ser Gly Lys Leu Glu Thr Tyr Ser Glu Gly Ser Ser Val
           130          135          140
Val Tyr Met Lys Ser Asn Gly Lys Gly Tyr Ile Val Thr Asn Asn His
           145          150          155          160
Val Ile Ser Gly Ser Asp Ala Val Gln Val Gln Leu Ala Asn Gly Lys
           165          170          175
Thr Val Ser Ala Lys Val Val Gly Lys Asp Ser Thr Thr Asp Leu Ala
           180          185          190
Val Leu Ser Ile Asp Ala Lys Tyr Val Thr Gln Thr Ala Glu Phe Gly
           195          200          205
Asp Ser Lys Ser Leu Gln Ala Gly Gln Thr Val Ile Ala Val Gly Ser
           210          215          220
Pro Leu Gly Ser Glu Tyr Ala Ser Thr Val Thr Gln Gly Ile Ile Ser
           225          230          235          240
Ala Pro Ala Arg Thr Ile Ser Thr Ser Ser Gly Asn Gln Gln Thr Val
           245          250          255
Ile Gln Thr Asp Ala Ala Ile Asn Pro Gly Asn Ser Gly Gly Ala Leu
           260          265          270
Val Asn Ser Ala Gly Gln Val Ile Gly Ile Asn Ser Met Lys Leu Ala
           275          280          285
Gln Ser Ser Asp Gly Thr Ser Val Glu Gly Met Gly Phe Ala Ile Pro
           290          295          300
Ser Asn Glu Val Val Thr Ile Val Asn Glu Leu Val Lys Lys Gly Lys
           305          310          315          320
Ile Thr Arg Pro Gln Leu Gly Val Arg Val Val Ala Leu Glu Gly Ile

```



-continued

---

	325		330		335										
Pro	Glu	Ala	Tyr	Arg	Ser	Arg	Leu	Lys	Ile	Lys	Ser	Asn	Leu	Lys	Ser
			340					345					350		
Gly	Ile	Tyr	Val	Ala	Ser	Ile	Asn	Lys	Asn	Ser	Ser	Ala	Ala	Asn	Ala
		355					360					365			
Gly	Met	Lys	Ser	Gly	Asp	Val	Ile	Thr	Lys	Val	Asp	Gly	Lys	Lys	Val
	370					375					380				
Asp	Asp	Val	Ala	Ser	Leu	His	Ser	Ile	Leu	Tyr	Ser	His	Lys	Val	Gly
	385				390					395					400
Asp	Thr	Val	Asn	Ile	Thr	Ile	Asn	Arg	Asn	Gly	Arg	Asp	Val	Asn	Leu
			405						410					415	
Lys	Val	Lys	Leu	Glu	Gly	Asn									
			420												

&lt;210&gt; SEQ ID NO 10

&lt;211&gt; LENGTH: 411

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Streptococcus thermophilus

&lt;400&gt; SEQUENCE: 10

Met	Lys	Lys	Phe	Asn	Trp	Lys	Lys	Ile	Val	Ala	Pro	Ile	Ala	Met	Leu
1				5					10						15
Ile	Ile	Gly	Leu	Leu	Gly	Gly	Leu	Leu	Gly	Ala	Phe	Ile	Leu	Leu	Thr
			20					25					30		
Ala	Ala	Gly	Val	Ser	Phe	Thr	Asn	Thr	Thr	Asp	Thr	Gly	Val	Lys	Thr
		35					40					45			
Ala	Lys	Thr	Val	Tyr	Thr	Asn	Ile	Thr	Asp	Thr	Thr	Lys	Ala	Val	Lys
	50					55					60				
Lys	Val	Gln	Asn	Ala	Val	Val	Ser	Val	Ile	Asn	Tyr	Gln	Glu	Gly	Ser
	65				70					75					80
Ser	Ser	Asp	Ser	Leu	Asn	Asp	Leu	Tyr	Gly	Arg	Ile	Phe	Gly	Gly	Gly
				85					90					95	
Asp	Ser	Ser	Asp	Ser	Ser	Gln	Glu	Asn	Ser	Lys	Asp	Ser	Asp	Gly	Leu
			100					105					110		
Gln	Val	Ala	Gly	Glu	Gly	Ser	Gly	Val	Ile	Tyr	Lys	Lys	Asp	Gly	Lys
		115					120					125			
Glu	Ala	Tyr	Ile	Val	Thr	Asn	Asn	His	Val	Val	Asp	Gly	Ala	Lys	Lys
	130					135					140				
Leu	Glu	Ile	Met	Leu	Ser	Asp	Gly	Ser	Lys	Ile	Thr	Gly	Glu	Leu	Val
	145				150					155					160
Gly	Lys	Asp	Thr	Tyr	Ser	Asp	Leu	Ala	Val	Val	Lys	Val	Ser	Ser	Asp
			165						170					175	
Lys	Ile	Thr	Thr	Val	Ala	Glu	Phe	Ala	Asp	Ser	Asn	Ser	Leu	Thr	Val
			180					185					190		
Gly	Glu	Lys	Ala	Ile	Ala	Ile	Gly	Ser	Pro	Leu	Gly	Thr	Glu	Tyr	Ala
		195					200					205			
Asn	Ser	Val	Thr	Glu	Gly	Ile	Val	Ser	Ser	Leu	Ser	Arg	Thr	Ile	Thr
	210					215					220				
Met	Gln	Asn	Asp	Asn	Gly	Glu	Thr	Val	Ser	Thr	Asn	Ala	Ile	Gln	Thr
	225				230					235					240
Asp	Ala	Ala	Ile	Asn	Pro	Gly	Asn	Ser	Gly	Gly	Ala	Leu	Val	Asn	Ile
				245					250					255	
Glu	Gly	Gln	Val	Ile	Gly	Ile	Asn	Ser	Ser	Lys	Ile	Ser	Ser	Thr	Ser
			260					265						270	
Ala	Val	Ala	Gly	Ser	Ala	Val	Glu	Gly	Met	Gly	Phe	Ala	Ile	Pro	Ser

-continued

275	280	285
Asn Asp Val Val Glu Ile Ile Asn Gln Leu Glu Lys Asp Gly Lys Val 290 295 300		
Thr Arg Pro Ala Leu Gly Ile Ser Ile Ala Asp Leu Asn Ser Leu Ser 305 310 315 320		
Ser Ser Ala Thr Ser Lys Leu Asp Leu Pro Asp Glu Val Lys Ser Gly 325 330 335		
Val Val Val Gly Ser Val Gln Lys Gly Met Pro Ala Asp Gly Lys Leu 340 345 350		
Gln Glu Tyr Asp Val Ile Thr Glu Ile Asp Gly Lys Lys Ile Ser Ser 355 360 365		
Lys Thr Asp Ile Gln Thr Asn Leu Tyr Ser His Ser Ile Gly Asp Thr 370 375 380		
Ile Lys Val Thr Phe Tyr Arg Gly Lys Asp Lys Lys Thr Val Asp Leu 385 390 395 400		
Lys Leu Thr Lys Ser Thr Glu Asp Ile Ser Asp 405 410		

&lt;210&gt; SEQ ID NO 11

&lt;211&gt; LENGTH: 16

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

&lt;400&gt; SEQUENCE: 11

aaagttcagc agcaag

16

&lt;210&gt; SEQ ID NO 12

&lt;211&gt; LENGTH: 18

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

&lt;400&gt; SEQUENCE: 12

ccggcagttt gttgggtg

18

&lt;210&gt; SEQ ID NO 13

&lt;211&gt; LENGTH: 18

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

&lt;400&gt; SEQUENCE: 13

ggcaaaagct aatatagg

18

&lt;210&gt; SEQ ID NO 14

&lt;211&gt; LENGTH: 16

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer

&lt;400&gt; SEQUENCE: 14

gtattgacat ttaccg

16

&lt;210&gt; SEQ ID NO 15

-continued

---

<211> LENGTH: 23  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer  
  
 <400> SEQUENCE: 15  
  
 tgtgggccct tttaaattggg cag 23

<210> SEQ ID NO 16  
 <211> LENGTH: 69  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic primer  
  
 <400> SEQUENCE: 16  
  
 gagatctcta atgatgatga tgatgatgaa cctcttgga caagtgaacc tgtgattttt 60  
 tcaatcacg 69

<210> SEQ ID NO 17  
 <211> LENGTH: 1224  
 <212> TYPE: DNA  
 <213> ORGANISM: Lactococcus lactis  
  
 <400> SEQUENCE: 17  
  
 atggcaaaag ctaatatagg aaaattgcta ttaaccggcg ttgtgggtgg agctatcgca 60  
 ctccgaggaa gcgcaattta tcaaagcact acaaaccaac taggaaatgc taaccgctca 120  
 aatcagacta gcacaaagg tagtaatggt tccgtaaagt tcaataccga tgttacctct 180  
 gcaattaaaa aagtttcaaa ttctgtcggt tctgttatga attatcaaaa acagaattca 240  
 caaagtgatt ttagttcaat ttttggtgga aatagcggct caagttcagc taatgacggc 300  
 ttgcaacttt ccagtgaggg ttctggtggt atttacaata aatctggtgg agatgcttac 360  
 gtggctcacta actatcacgt tattgccgga aatagttccc tcgatgtttt actttctggt 420  
 gggcaaaaag ttaaagccac agttggtggt tatgatgaat aactgacct tgcggttctt 480  
 aaaatcagct ctgacctgt taaagacgtg gcaactttcg ctgattcaag caagttaact 540  
 atggtgaac cagctattgc agtcggctca ccttaggta gccagtttgc taatactgca 600  
 accgaaggaa ttctgtctgc aacaagtcgt caagtcactt tgactcaaga aaatgggtcaa 660  
 acaacaagta tcaatgcgat tcaaacggat gctgccatta accctggtaa ctcaggtgga 720  
 gccttgatta atattgaagg tcaagtgatt ggtattactc aaagtaaaat cacaacgact 780  
 gaagatggtt ctacctctgt ggaaggttta ggttttgcta tcccatctaa tgatgtggta 840  
 aacatcatta ataaacttga aactgatggt aagatttcac gtccctgcctt aggtattcgt 900  
 atggttgacc tatctcaatt atcaacaaat gatagttctc aactgaaatt acctagcagc 960  
 gtaactgggtg gagtgggtgt ctactctggt caagcgggtc ttctgctgc cacagctggt 1020  
 ctgaaagctg gcgatgtgat aacgaaggtg ggagataccg ccgttacttc atcaacagac 1080  
 ttacaaagtg ctctttactc acacaatatt aatgatactg tgaaagtcac ctactaccgt 1140  
 gatggtaaat cagccacagc aaatgtcaaa ctctctaaat caacaagcga tttagaaaca 1200  
 aatagtccat cttcttctaa ttaa 1224

<210> SEQ ID NO 18  
 <211> LENGTH: 1902  
 <212> TYPE: PRT

-continued

<213> ORGANISM: *Lactococcus lactis*

&lt;400&gt; SEQUENCE: 18

Met Gln Arg Lys Lys Lys Gly Leu Ser Ile Leu Leu Ala Gly Thr Val  
 1 5 10 15  
 Ala Leu Gly Ala Leu Ala Val Leu Pro Val Gly Glu Ile Gln Ala Lys  
 20 25 30  
 Ala Ala Ile Ser Gln Gln Thr Lys Gly Ser Ser Leu Ala Asn Thr Val  
 35 40 45  
 Thr Ala Ala Thr Ala Lys Gln Ala Ala Thr Asp Thr Thr Ala Ala Thr  
 50 55 60  
 Thr Asn Gln Ala Ile Ala Thr Gln Leu Ala Ala Lys Gly Ile Asp Tyr  
 65 70 75 80  
 Asn Lys Leu Asn Lys Val Gln Gln Gln Asp Ile Tyr Val Asp Val Ile  
 85 90 95  
 Val Gln Met Ser Ala Ala Pro Ala Ser Glu Asn Gly Ile Leu Arg Thr  
 100 105 110  
 Asp Tyr Ser Ser Thr Ala Glu Ile Gln Gln Glu Thr Asn Lys Val Ile  
 115 120 125  
 Ala Ala Gln Ala Ser Val Lys Ala Ala Val Glu Gln Val Thr Gln Gln  
 130 135 140  
 Thr Ala Gly Glu Ser Tyr Gly Tyr Val Val Asn Gly Phe Ser Thr Lys  
 145 150 155 160  
 Val Arg Val Val Asp Ile Pro Lys Leu Lys Gln Ile Ala Gly Val Lys  
 165 170 175  
 Thr Val Thr Leu Ala Lys Val Tyr Tyr Pro Thr Asp Ala Lys Ala Asn  
 180 185 190  
 Ser Met Ala Asn Val Gln Ala Val Trp Ser Asn Tyr Lys Tyr Lys Gly  
 195 200 205  
 Glu Gly Thr Val Val Ser Val Ile Asp Ser Gly Ile Asp Pro Thr His  
 210 215 220  
 Lys Asp Met Arg Leu Ser Asp Asp Lys Asp Val Lys Leu Thr Lys Ser  
 225 230 235 240  
 Asp Val Glu Lys Phe Thr Asp Thr Val Lys His Gly Arg Tyr Phe Asn  
 245 250 255  
 Ser Lys Val Pro Tyr Gly Phe Asn Tyr Ala Asp Asn Asn Asp Thr Ile  
 260 265 270  
 Thr Asp Asp Lys Val Asp Glu Gln His Gly Met His Val Ala Gly Ile  
 275 280 285  
 Ile Gly Ala Asn Gly Thr Gly Asp Asp Pro Ala Lys Ser Val Val Gly  
 290 295 300  
 Val Ala Pro Glu Ala Gln Leu Leu Ala Met Lys Val Phe Ser Asn Ser  
 305 310 315 320  
 Asp Thr Ser Ala Lys Thr Gly Ser Ala Thr Val Val Ser Ala Ile Glu  
 325 330 335  
 Asp Ser Ala Lys Ile Gly Ala Asp Val Leu Asn Met Ser Leu Gly Ser  
 340 345 350  
 Asn Ser Gly Asn Gln Thr Leu Glu Asp Pro Glu Leu Ala Ala Val Gln  
 355 360 365  
 Asn Ala Asn Glu Ser Gly Thr Ala Ala Val Ile Ser Ala Gly Asn Ser  
 370 375 380  
 Gly Thr Ser Gly Ser Ala Thr Glu Gly Val Asn Lys Asp Tyr Tyr Gly  
 385 390 395 400  
 Leu Gln Asp Asn Glu Met Val Gly Ser Pro Gly Thr Ser Arg Gly Ala

-continued

405					410					415					
Thr	Thr	Val	Ala	Ser	Ala	Glu	Asn	Thr	Asp	Val	Ile	Thr	Gln	Ala	Val
			420					425					430		
Thr	Ile	Thr	Asp	Gly	Thr	Gly	Leu	Gln	Leu	Gly	Pro	Glu	Thr	Ile	Gln
		435					440					445			
Leu	Ser	Ser	His	Asp	Phe	Thr	Gly	Ser	Phe	Asp	Gln	Lys	Lys	Phe	Tyr
	450					455					460				
Ile	Val	Lys	Asp	Ala	Ser	Gly	Asn	Leu	Ser	Lys	Gly	Ala	Leu	Ala	Asp
465						470					475				480
Tyr	Thr	Ala	Asp	Ala	Lys	Gly	Lys	Ile	Ala	Ile	Val	Lys	Arg	Gly	Glu
				485					490					495	
Phe	Ser	Phe	Asp	Asp	Lys	Gln	Lys	Tyr	Ala	Gln	Ala	Ala	Gly	Ala	Ala
			500					505					510		
Gly	Leu	Ile	Ile	Val	Asn	Thr	Asp	Gly	Thr	Ala	Thr	Pro	Met	Thr	Ser
		515					520					525			
Ile	Ala	Leu	Thr	Thr	Thr	Phe	Pro	Thr	Phe	Gly	Leu	Ser	Ser	Val	Thr
	530					535					540				
Gly	Gln	Lys	Leu	Val	Asp	Trp	Val	Thr	Ala	His	Pro	Asp	Asp	Ser	Leu
545						550					555				560
Gly	Val	Lys	Ile	Thr	Leu	Ala	Met	Leu	Pro	Asn	Gln	Lys	Tyr	Thr	Glu
				565					570					575	
Asp	Lys	Met	Ser	Asp	Phe	Thr	Ser	Tyr	Gly	Pro	Val	Ser	Asn	Leu	Ser
			580					585					590		
Phe	Lys	Pro	Asp	Ile	Thr	Ala	Pro	Gly	Gly	Asn	Ile	Trp	Ser	Thr	Gln
		595					600					605			
Asn	Asn	Asn	Gly	Tyr	Thr	Asn	Met	Ser	Gly	Thr	Ser	Met	Ala	Ser	Pro
	610					615					620				
Phe	Ile	Ala	Gly	Ser	Gln	Ala	Leu	Leu	Lys	Gln	Ala	Leu	Asn	Asn	Lys
625						630					635				640
Asn	Asn	Pro	Phe	Tyr	Ala	Tyr	Tyr	Lys	Gln	Leu	Lys	Gly	Thr	Ala	Leu
				645					650					655	
Thr	Asp	Phe	Leu	Lys	Thr	Val	Glu	Met	Asn	Thr	Ala	Gln	Pro	Ile	Asn
			660					665					670		
Asp	Ile	Asn	Tyr	Asn	Asn	Val	Ile	Val	Ser	Pro	Arg	Arg	Gln	Gly	Ala
	675					680					685				
Gly	Leu	Val	Asp	Val	Lys	Ala	Ala	Ile	Asp	Ala	Leu	Glu	Lys	Asn	Pro
	690					695					700				
Ser	Thr	Val	Val	Ala	Glu	Asn	Gly	Tyr	Pro	Ala	Val	Glu	Leu	Lys	Asp
705						710					715				720
Phe	Thr	Ser	Thr	Asp	Lys	Thr	Phe	Lys	Leu	Thr	Phe	Thr	Asn	Arg	Thr
				725					730					735	
Thr	His	Glu	Leu	Thr	Tyr	Gln	Met	Asp	Ser	Asn	Thr	Asp	Thr	Asn	Ala
			740					745					750		
Val	Tyr	Thr	Ser	Ala	Thr	Asp	Pro	Asn	Ser	Gly	Val	Leu	Tyr	Asp	Lys
		755					760					765			
Lys	Ile	Asp	Gly	Ala	Ala	Ile	Lys	Ala	Gly	Ser	Asn	Ile	Thr	Val	Pro
	770					775					780				
Ala	Gly	Lys	Thr	Ala	Gln	Ile	Glu	Phe	Thr	Leu	Ser	Leu	Pro	Lys	Ser
785						790					795				800
Phe	Asp	Gln	Gln	Gln	Phe	Val	Glu	Gly	Phe	Leu	Asn	Phe	Lys	Gly	Ser
				805					810					815	
Asp	Gly	Ser	Arg	Leu	Asn	Leu	Pro	Tyr	Met	Gly	Phe	Phe	Gly	Asp	Trp
			820					825					830		

-continued

---

Asn	Asp	Gly	Lys	Ile	Val	Asp	Ser	Leu	Asn	Gly	Ile	Thr	Tyr	Ser	Pro
		835					840						845		
Ala	Gly	Gly	Asn	Phe	Gly	Thr	Val	Pro	Leu	Leu	Lys	Asn	Lys	Asn	Thr
		850					855					860			
Gly	Thr	Gln	Tyr	Tyr	Gly	Gly	Met	Val	Thr	Asp	Ala	Asp	Gly	Asn	Lys
		865				870					875				880
Thr	Val	Asp	Asp	Gln	Ala	Ile	Ala	Phe	Ser	Ser	Asp	Lys	Asn	Ala	Leu
				885					890					895	
Tyr	Asn	Asp	Ile	Ser	Met	Lys	Tyr	Tyr	Leu	Leu	Arg	Asn	Ile	Ser	Asn
			900						905				910		
Val	Gln	Val	Asp	Ile	Leu	Asp	Gly	Gln	Gly	Asn	Lys	Val	Thr	Thr	Leu
			915					920					925		
Ser	Ser	Ser	Thr	Asn	Arg	Lys	Lys	Thr	Tyr	Tyr	Asn	Ala	His	Ser	Gln
		930					935				940				
Gln	Tyr	Ile	Tyr	Tyr	Asn	Ala	Pro	Ala	Trp	Asp	Gly	Thr	Tyr	Tyr	Asp
					950						955				960
Gln	Arg	Asp	Gly	Asn	Ile	Lys	Thr	Ala	Asp	Asp	Gly	Ser	Tyr	Thr	Tyr
				965					970						975
Arg	Ile	Ser	Gly	Val	Pro	Glu	Gly	Gly	Asp	Lys	Arg	Gln	Val	Phe	Asp
			980						985					990	
Val	Pro	Phe	Lys	Leu	Asp	Ser	Lys	Ala	Pro	Thr	Val	Arg	His	Val	Ala
			995				1000						1005		
Leu	Ser	Ala	Lys	Thr	Glu	Asn	Gly	Lys	Thr	Gln	Tyr	Tyr	Leu	Thr	Ala
						1015					1020				
Glu	Ala	Lys	Asp	Asp	Leu	Ser	Gly	Leu	Asp	Ala	Thr	Lys	Ser	Val	Lys
					1030					1035					1040
Thr	Glu	Ile	Asn	Glu	Val	Thr	Asn	Leu	Asp	Ala	Thr	Phe	Thr	Asp	Ala
				1045					1050					1055	
Gly	Thr	Thr	Ala	Asp	Gly	Tyr	Thr	Lys	Ile	Glu	Thr	Pro	Leu	Ser	Asp
			1060					1065					1070		
Glu	Gln	Ala	Gln	Ala	Leu	Gly	Asn	Gly	Asp	Asn	Ser	Ala	Glu	Leu	Tyr
		1075					1080					1085			
Leu	Thr	Asp	Asn	Ala	Ser	Asn	Ala	Thr	Asp	Gln	Asp	Ala	Ser	Val	Gln
		1090				1095					1100				
Lys	Pro	Gly	Ser	Thr	Ser	Phe	Asp	Leu	Ile	Val	Asn	Gly	Gly	Gly	Ile
					1110					1115					1120
Pro	Asp	Lys	Ile	Ser	Ser	Thr	Thr	Thr	Gly	Tyr	Glu	Ala	Asn	Thr	Gln
				1125					1130					1135	
Gly	Gly	Gly	Thr	Tyr	Thr	Phe	Ser	Gly	Thr	Tyr	Pro	Ala	Ala	Val	Asp
			1140					1145					1150		
Gly	Thr	Tyr	Thr	Asp	Ala	Gln	Gly	Lys	Lys	His	Asp	Leu	Asn	Thr	Thr
		1155					1160					1165			
Tyr	Asp	Ala	Ala	Thr	Asn	Ser	Phe	Thr	Ala	Ser	Met	Pro	Val	Thr	Asn
		1170				1175					1180				
Ala	Asp	Tyr	Ala	Ala	Gln	Val	Asp	Leu	Tyr	Ala	Asp	Lys	Ala	His	Thr
					1190					1195					1200
Gln	Leu	Leu	Lys	His	Phe	Asp	Thr	Lys	Val	Arg	Leu	Met	Ala	Pro	Thr
				1205					1210						1215
Phe	Thr	Asp	Leu	Lys	Phe	Asn	Asn	Gly	Ser	Asp	Gln	Thr	Ser	Glu	Ala
			1220					1225					1230		
Thr	Ile	Lys	Val	Thr	Gly	Thr	Val	Ser	Ala	Asp	Thr	Lys	Thr	Val	Asn
		1235					1240					1245			
Val	Gly	His	Thr	Val	Ala	Ala	Leu	Asp	Ala	Gln	His	His	Phe	Ser	Val
						1255					1260				

-continued

---

Asp Val Pro Val Asn Tyr Gly Asp Asn Thr Ile Lys Val Thr Ala Thr  
 1265 1270 1275 1280

Asp Lys Asp Gly Asn Thr Thr Thr Glu Gln Lys Thr Ile Thr Ser Ser  
 1285 1290 1295

Tyr Asp Pro Asp Met Leu Lys Lys Ser Val Thr Phe Asp Gln Gly Val  
 1300 1305 1310

Lys Phe Gly Thr Asn Lys Phe Asn Ala Thr Ser Ala Lys Phe Tyr Asp  
 1315 1320 1325

Pro Lys Thr Gly Ile Ala Thr Ile Thr Gly Lys Val Lys His Pro Thr  
 1330 1335 1340

Thr Thr Leu Gln Val Asp Gly Lys Gln Ile Pro Ile Lys Asp Asp Leu  
 1345 1350 1355 1360

Thr Phe Ser Phe Thr Leu Asp Leu Gly Thr Leu Gly Gln Lys Pro Phe  
 1365 1370 1375

Gly Val Val Val Gly Asp Thr Thr Gln Asn Lys Thr Phe Gln Glu Ala  
 1380 1385 1390

Leu Ser Phe Ile Leu Asp Ala Val Ala Pro Thr Leu Ser Leu Asp Ser  
 1395 1400 1405

Ser Thr Asp Ala Pro Val Tyr Thr Asn Asp Pro Asn Phe Gln Ile Thr  
 1410 1415 1420

Gly Thr Ala Thr Asp Asn Ala Gln Tyr Leu Ser Leu Ser Ile Asn Gly  
 1425 1430 1435 1440

Ser Ser Val Ala Ser Gln Tyr Glu Asp Ile Asn Ile Asn Ser Gly Lys  
 1445 1450 1455

Pro Gly His Met Ala Ile Asp Gln Pro Val Lys Leu Leu Glu Gly Lys  
 1460 1465 1470

Asn Val Leu Thr Val Ala Val Thr Asp Ser Glu Asp Asn Thr Thr Thr  
 1475 1480 1485

Lys Asn Ile Thr Val Tyr Tyr Glu Pro Lys Lys Thr Leu Ala Ala Pro  
 1490 1495 1500

Thr Val Thr Pro Ser Thr Thr Glu Pro Ala Gln Thr Val Thr Leu Thr  
 1505 1510 1515 1520

Ala Asn Ala Ala Ala Thr Gly Glu Thr Val Gln Tyr Ser Ala Asp Gly  
 1525 1530 1535

Gly Lys Thr Tyr Gln Asp Val Pro Ala Ala Gly Val Thr Ile Thr Ala  
 1540 1545 1550

Asn Gly Thr Phe Lys Phe Lys Ser Thr Asp Leu Tyr Gly Asn Glu Ser  
 1555 1560 1565

Pro Ala Val Asp Tyr Val Val Thr Asn Ile Lys Ala Asp Asp Pro Ala  
 1570 1575 1580

Gln Leu Gln Ala Ala Lys Gln Glu Leu Thr Asn Leu Ile Ala Ser Ala  
 1585 1590 1595 1600

Lys Thr Leu Ser Ala Ser Gly Lys Tyr Asp Asp Ala Thr Thr Thr Ala  
 1605 1610 1615

Leu Ala Ala Ala Thr Gln Lys Ala Gln Thr Ala Leu Asp Gln Thr Asn  
 1620 1625 1630

Ala Ser Val Asp Ser Leu Thr Gly Ala Asn Arg Asp Leu Gln Thr Ala  
 1635 1640 1645

Ile Asn Gln Leu Ala Ala Lys Leu Pro Ala Asp Lys Lys Thr Ser Leu  
 1650 1655 1660

Leu Asn Gln Leu Gln Ser Val Lys Asp Ala Leu Gly Thr Asp Leu Gly  
 1665 1670 1675 1680

Asn Gln Thr Asp Pro Ser Thr Gly Lys Thr Phe Thr Ala Ala Leu Asp

-continued

1685	1690	1695
Asp Leu Val Ala Gln Ala Gln Ala Gly Thr Gln Thr Asp Asp Gln Leu 1700 1705 1710		
Gln Ala Thr Leu Ala Lys Ile Leu Asp Glu Val Leu Ala Lys Leu Ala 1715 1720 1725		
Glu Gly Ile Lys Ala Ala Thr Pro Ala Glu Val Gly Asn Ala Lys Asp 1730 1735 1740		
Ala Ala Thr Gly Lys Thr Trp Tyr Ala Asp Ile Ala Asp Thr Leu Thr 1745 1750 1755 1760		
Ser Gly Gln Ala Ser Ala Asp Ala Ser Asp Lys Leu Ala His Leu Gln 1765 1770 1775		
Ala Leu Gln Ser Leu Lys Thr Lys Val Ala Ala Ala Val Glu Ala Ala 1780 1785 1790		
Lys Thr Val Gly Lys Gly Asp Gly Thr Thr Gly Thr Ser Asp Lys Gly 1795 1800 1805		
Gly Gly Gln Gly Thr Pro Ala Pro Ala Pro Gly Asp Thr Gly Lys Asp 1810 1815 1820		
Lys Gly Asp Glu Gly Ser Gln Pro Ser Ser Gly Gly Asn Ile Pro Thr 1825 1830 1835 1840		
Lys Pro Ala Thr Thr Thr Ser Thr Thr Thr Asp Asp Thr Thr Asp Arg 1845 1850 1855		
Asn Gly Gln Leu Thr Ser Gly Lys Gly Ala Leu Pro Lys Thr Gly Glu 1860 1865 1870		
Thr Thr Glu Arg Pro Ala Phe Gly Phe Leu Gly Val Ile Val Val Ser 1875 1880 1885		
Leu Met Gly Val Leu Gly Leu Lys Arg Lys Gln Arg Glu Glu 1890 1895 1900		

&lt;210&gt; SEQ ID NO 19

&lt;211&gt; LENGTH: 744

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Lactococcus lactis

&lt;220&gt; FEATURE:

&lt;221&gt; NAME/KEY: MOD\_RES

&lt;222&gt; LOCATION: (374)

&lt;223&gt; OTHER INFORMATION: variable amino acid

&lt;220&gt; FEATURE:

&lt;221&gt; NAME/KEY: MOD\_RES

&lt;222&gt; LOCATION: (744)

&lt;223&gt; OTHER INFORMATION: variable amino acid

&lt;400&gt; SEQUENCE: 19

Met Gln Arg Lys Lys Lys Gly Leu Ser Ile Leu Leu Ala Gly Thr Val 1 5 10 15
Ala Leu Gly Ala Leu Ala Val Leu Pro Val Gly Glu Ile Gln Ala Lys 20 25 30
Ala Ala Ile Ser Gln Gln Thr Lys Gly Ser Ser Leu Ala Asn Thr Val 35 40 45
Thr Ala Ala Thr Ala Lys Gln Ala Ala Thr Asp Thr Thr Ala Ala Thr 50 55 60
Thr Asn Gln Ala Ile Ala Thr Gln Leu Ala Ala Lys Gly Ile Asp Tyr 65 70 75 80
Asn Lys Leu Asn Lys Val Gln Gln Gln Asp Ile Tyr Val Asp Val Ile 85 90 95
Val Gln Met Ser Ala Ala Pro Ala Ser Glu Asn Gly Thr Leu Arg Thr 100 105 110
Asp Tyr Ser Ser Thr Ala Glu Ile Gln Gln Glu Thr Asn Lys Val Ile 115 120 125



-continued

---

Ala Ala Gln Ala Ser Val Lys Ala Ala Val Glu Gln Val Thr Gln Gln  
130 135 140

Thr Ala Gly Glu Ser Tyr Gly Tyr Val Val Asn Gly Phe Ser Thr Lys  
145 150 155 160

Val Arg Val Val Asp Ile Pro Lys Leu Lys Gln Ile Ala Gly Val Lys  
165 170 175

Thr Val Thr Leu Ala Lys Val Tyr Tyr Pro Thr Asp Ala Lys Ala Asn  
180 185 190

Ser Met Ala Asn Val Gln Ala Val Trp Ser Asn Tyr Lys Tyr Lys Gly  
195 200 205

Glu Gly Thr Val Val Ser Val Ile Asp Ser Gly Ile Asp Pro Thr His  
210 215 220

Lys Asp Met Arg Leu Ser Asp Asp Lys Asp Val Lys Leu Thr Lys Ser  
225 230 235 240

Asp Val Glu Lys Phe Thr Asp Thr Ala Lys His Gly Arg Tyr Phe Asn  
245 250 255

Ser Lys Val Pro Tyr Gly Phe Asn Tyr Ala Asp Asn Asn Asp Thr Ile  
260 265 270

Thr Asp Asp Thr Val Asp Glu Gln His Gly Met His Val Ala Gly Ile  
275 280 285

Ile Gly Ala Asn Gly Thr Gly Asp Asp Pro Ala Lys Ser Val Val Gly  
290 295 300

Val Ala Pro Glu Ala Gln Leu Leu Ala Met Lys Val Phe Thr Asn Ser  
305 310 315 320

Asp Thr Ser Ala Thr Thr Gly Ser Ala Thr Leu Val Ser Ala Ile Glu  
325 330 335

Asp Ser Ala Lys Ile Gly Ala Asp Val Leu Asn Met Ser Leu Gly Ser  
340 345 350

Asp Ser Gly Asn Gln Thr Leu Glu Asp Pro Glu Leu Ala Ala Val Gln  
355 360 365

Asn Ala Asn Glu Ser Xaa Thr Ala Ala Val Ile Ser Ala Gly Asn Ser  
370 375 380

Gly Thr Ser Gly Ser Ala Thr Glu Gly Val Asn Lys Asp Tyr Tyr Gly  
385 390 395 400

Leu Gln Asp Asn Glu Met Val Gly Thr Pro Gly Thr Ser Arg Gly Ala  
405 410 415

Thr Thr Val Ala Ser Ala Glu Asn Thr Asp Val Ile Thr Gln Ala Val  
420 425 430

Thr Ile Thr Asp Gly Thr Gly Leu Gln Leu Gly Pro Glu Thr Ile Gln  
435 440 445

Leu Ser Ser Asn Asp Phe Thr Gly Ser Phe Asp Gln Lys Lys Phe Tyr  
450 455 460

Val Val Lys Asp Ala Ser Gly Asn Leu Ser Lys Gly Lys Val Ala Asp  
465 470 475 480

Tyr Thr Ala Asp Ala Lys Gly Lys Ile Ala Ile Val Lys Arg Gly Glu  
485 490 495

Leu Thr Phe Ala Asp Lys Gln Lys Tyr Ala Gln Ala Ala Gly Ala Ala  
500 505 510

Gly Leu Ile Ile Val Asn Asn Asp Gly Thr Ala Thr Pro Val Thr Ser  
515 520 525

Met Ala Leu Thr Thr Thr Phe Pro Thr Phe Gly Leu Ser Ser Val Thr  
530 535 540

Gly Gln Lys Leu Val Asp Trp Val Ala Ala His Pro Asp Asp Ser Leu

-continued

545	550	555	560
Gly Val Lys Ile Ala Leu Thr Leu Val Pro Asn Gln Lys Tyr Thr Glu	565	570	575
Asp Lys Met Ser Asp Phe Thr Ser Tyr Gly Pro Val Ser Asn Leu Ser	580	585	590
Phe Lys Pro Asp Ile Thr Ala Pro Gly Gly Asn Ile Trp Ser Thr Gln	595	600	605
Asn Asn Asn Gly Tyr Thr Asn Met Ser Gly Thr Ser Met Ala Ser Pro	610	615	620
Phe Ile Ala Gly Ser Gln Ala Leu Leu Lys Gln Ala Leu Asn Asn Lys	625	630	635
Asn Asn Pro Phe Tyr Ala Tyr Tyr Lys Gln Leu Lys Gly Thr Ala Leu	645	650	655
Thr Asp Phe Leu Lys Thr Val Glu Met Asn Thr Ala Gln Pro Ile Asn	660	665	670
Asp Ile Asn Tyr Asn Asn Val Ile Val Ser Pro Arg Arg Gln Gly Ala	675	680	685
Gly Leu Val Asp Val Lys Ala Ala Ile Asp Ala Leu Glu Lys Asn Pro	690	695	700
Ser Thr Val Val Ala Glu Asn Gly Tyr Pro Ala Val Glu Leu Lys Asp	705	710	715
Phe Thr Ser Thr Asp Lys Thr Phe Lys Leu Thr Phe Thr Asn Arg Thr	725	730	735
Thr His Glu Leu Thr Tyr Gln Xaa	740		
<210> SEQ ID NO 20			
<211> LENGTH: 264			
<212> TYPE: PRT			
<213> ORGANISM: Lactococcus lactis			
<400> SEQUENCE: 20			
Ala Ala Ala Thr Gln Lys Ala Gln Thr Ala Leu Asp Gln Thr Asn Ala	1	5	10
Ser Val Asp Ser Leu Thr Gly Ala Asn Arg Asp Leu Gln Thr Ala Ile	20	25	30
Asn Gln Leu Ala Ala Lys Leu Pro Ala Asp Lys Lys Thr Ser Leu Leu	35	40	45
Asn Gln Leu Gln Ser Val Lys Ala Ala Leu Glu Thr Asp Leu Gly Asn	50	55	60
Gln Thr Asp Ser Ser Thr Gly Lys Thr Phe Thr Ala Ala Leu Asp Asp	65	70	75
Leu Val Ala Gln Ala Gln Ala Gly Thr Gln Thr Asp Asp Gln Leu Gln	85	90	95
Ala Thr Leu Ala Lys Val Leu Asp Ala Val Leu Ala Lys Leu Ala Glu	100	105	110
Gly Ile Lys Ala Ala Thr Pro Ala Glu Val Gly Asn Ala Lys Asp Ala	115	120	125
Ala Thr Gly Lys Thr Trp Tyr Ala Asp Ile Ala Asp Thr Leu Thr Ser	130	135	140
Gly Gln Ala Ser Ala Asp Ala Ser Asp Lys Leu Ala His Leu Gln Ala	145	150	155
Leu Gln Ser Leu Lys Thr Lys Val Ala Ala Val Glu Ala Ala Lys	165	170	175
Thr Val Gly Lys Gly Asp Gly Thr Thr Gly Thr Ser Asp Lys Gly Gly			



-continued

290				295				300							
Asn	Gly	Thr	Gly	Asp	Asp	Pro	Thr	Lys	Ser	Val	Val	Gly	Val	Ala	Pro
305					310					315					320
Glu	Ala	Gln	Leu	Leu	Ala	Met	Lys	Val	Phe	Thr	Asn	Ser	Asp	Thr	Ser
				325					330					335	
Ala	Thr	Thr	Gly	Ser	Ala	Thr	Leu	Val	Ser	Ala	Ile	Glu	Asp	Ser	Ala
			340					345					350		
Lys	Ile	Gly	Ala	Asp	Val	Leu	Asn	Met	Ser	Leu	Gly	Ser	Asp	Ser	Gly
		355					360					365			
Asn	Gln	Thr	Leu	Glu	Asp	Pro	Glu	Ile	Ala	Ala	Val	Gln	Asn	Ala	Asn
	370					375					380				
Glu	Ser	Gly	Thr	Ala	Ala	Val	Ile	Ser	Ala	Gly	Asn	Ala	Gly	Thr	Ser
385					390					395					400
Gly	Ser	Ala	Thr	Gln	Gly	Val	Asn	Lys	Asp	Tyr	Tyr	Gly	Leu	Gln	Asp
				405					410					415	
Asn	Glu	Met	Val	Gly	Thr	Pro	Gly	Thr	Ser	Arg	Gly	Ala	Thr	Thr	Val
			420					425					430		
Ala	Ser	Ala	Glu	Asn	Thr	Asp	Val	Ile	Ser	Gln	Ala	Val	Thr	Ile	Thr
		435					440					445			
Asp	Gly	Lys	Glu	Leu	Gln	Leu	Gly	Pro	Glu	Thr	Ile	Gln	Leu	Ser	Ser
	450					455					460				
Asn	Asp	Phe	Thr	Gly	Ser	Phe	Asp	Gln	Lys	Lys	Phe	Tyr	Val	Val	Lys
465					470					475					480
Asp	Ala	Ser	Gly	Asp	Leu	Ser	Lys	Gly	Ala	Ala	Ala	Asp	Tyr	Thr	Ala
				485				490						495	
Asp	Ala	Lys	Gly	Lys	Ile	Ala	Ile	Val	Lys	Arg	Gly	Glu	Leu	Thr	Phe
			500					505				510			
Ala	Asp	Lys	Gln	Lys	Tyr	Ala	Gln	Ala	Ala	Gly	Ala	Ala	Gly	Leu	Ile
		515					520					525			
Ile	Val	Asn	Asn	Asp	Gly	Thr	Ala	Thr	Pro	Leu	Thr	Ser	Ile	Thr	Leu
	530					535					540				
Thr	Thr	Thr	Phe	Pro	Thr	Phe	Gly	Leu	Ser	Ser	Val	Thr	Gly	Lys	Lys
545					550					555					560
Leu	Val	Asp	Trp	Val	Thr	Ala	His	Pro	Asp	Asp	Ser	Leu	Gly	Val	Lys
				565					570					575	
Ile	Ala	Leu	Thr	Leu	Leu	Pro	Asn	Gln	Lys	Tyr	Thr	Glu	Asp	Lys	Met
			580					585					590		
Ser	Asp	Phe	Thr	Ser	Tyr	Gly	Pro	Val	Ser	Asn	Leu	Ser	Phe	Lys	Pro
		595					600					605			
Asp	Ile	Thr	Ala	Pro	Gly	Gly	Asn	Ile	Trp	Ser	Thr	Gln	Asn	Asn	Asn
	610					615					620				
Gly	Tyr	Thr	Asn	Met	Ser	Gly	Thr	Ser	Met	Ala	Ser	Pro	Phe	Ile	Ala
625					630					635					640
Gly	Ser	Gln	Ala	Leu	Leu	Lys	Gln	Ala	Leu	Asn	Asn	Lys	Asn	Asn	Pro
				645					650					655	
Phe	Tyr	Ala	Asp	Tyr	Lys	Gln	Leu	Lys	Gly	Thr	Ala	Leu	Thr	Asp	Phe
			660					665					670		
Leu	Lys	Thr	Val	Glu	Met	Asn	Thr	Ala	Gln	Pro	Ile	Asn	Asp	Ile	Asn
		675					680					685			
Tyr	Asn	Asn	Val	Ile	Val	Ser	Pro	Arg	Arg	Gln	Gly	Ala	Gly	Leu	Val
	690					695					700				
Asp	Val	Lys	Ala	Ala	Ile	Asp	Ala	Leu	Glu	Lys	Asn	Pro	Ser	Thr	Val
705					710					715					720

-continued

Val	Ala	Glu	Asn	Gly	Tyr	Pro	Ala	Val	Glu	Leu	Lys	Asp	Phe	Thr	Ser
			725						730					735	
Thr	Asp	Lys	Thr	Phe	Lys	Leu	Thr	Phe	Thr	Asn	Arg	Thr	Thr	His	Glu
			740					745						750	
Leu	Thr	Tyr	Gln	Met	Asp	Ser	Asn	Thr	Asp	Thr	Asn	Ala	Val	Tyr	Thr
		755					760					765			
Ser	Ala	Thr	Asp	Pro	His	Ser	Gly	Val	Leu	Tyr	Asp	Lys	Lys	Ile	Asp
	770					775					780				
Gly	Ala	Ala	Ile	Lys	Ala	Gly	Ser	Asp	Ile	Thr	Val	Pro	Ala	Gly	Lys
785					790					795					800
Thr	Ala	Gln	Ile	Glu	Phe	Thr	Leu	Ser	Leu	Pro	Lys	Ser	Phe	Asp	Gln
				805					810					815	
Gln	Gln	Phe	Val	Glu	Gly	Phe	Leu	Asn	Phe	Lys	Gly	Ser	Asp	Gly	Ser
			820					825					830		
Arg	Leu	Asn	Leu	Pro	Tyr	Met	Gly	Phe	Phe	Gly	Asp	Trp	Asn	Asp	Gly
		835					840						845		
Lys	Ile	Val	Asp	Ser	Leu	Asn	Gly	Ile	Thr	Tyr	Ser	Pro	Ala	Gly	Gly
	850					855					860				
Asn	Tyr	Gly	Thr	Val	Pro	Leu	Leu	Thr	Asn	Lys	Asn	Thr	Gly	Asn	Gln
865					870					875					880
Tyr	Tyr	Gly	Gly	Met	Val	Thr	Asp	Ala	Asp	Gly	Asn	Gln	Thr	Val	Asp
				885					890					895	
Asp	Gln	Ala	Ile	Ala	Phe	Ser	Ser	Asp	Lys	Asn	Ala	Leu	Tyr	Asn	Asp
			900					905					910		
Ile	Ser	Met	Gln	Tyr	Tyr	Leu	Leu	Arg	Asn	Ile	Ser	Asn	Val	Gln	Val
		915					920					925			
Asp	Ile	Leu	Asp	Gly	Gln	Gly	Asn	Lys	Val	Thr	Thr	Leu	Ser	Ser	Ser
	930					935						940			
Thr	Asn	Gln	Thr	Lys	Thr	Tyr	Tyr	Asp	Ala	His	Ser	Arg	Lys	Tyr	Ile
945					950					955					960
Tyr	Tyr	Asn	Ala	Pro	Ala	Trp	Asp	Gly	Thr	Tyr	Tyr	Asp	Gln	Arg	Asp
				965					970					975	
Gly	Asn	Ile	Lys	Thr	Ala	Asp	Asp	Gly	Ser	Tyr	Thr	Tyr	Arg	Ile	Ser
		980						985					990		
Gly	Val	Pro	Glu	Gly	Gly	Asp	Lys	Arg	Gln	Val	Phe	Asp	Val	Pro	Phe
		995					1000					1005			
Lys	Leu	Asp	Ser	Lys	Ala	Pro	Thr	Val	Arg	His	Val	Ala	Leu	Ser	Ala
	1010					1015					1020				
Lys	Thr	Glu	Asn	Gly	Lys	Thr	Gln	Tyr	Tyr	Leu	Thr	Ala	Glu	Ala	Lys
1025					1030					1035					1040
Asp	Asp	Leu	Ser	Gly	Leu	Asp	Ala	Thr	Lys	Ser	Val	Lys	Thr	Ala	Ile
			1045						1050					1055	
Asn	Glu	Val	Thr	Asn	Leu	Asn	Ala	Thr	Phe	Thr	Asp	Ala	Gly	Thr	Thr
		1060						1065					1070		
Ala	Asp	Gly	Tyr	Thr	Lys	Ile	Glu	Thr	Pro	Leu	Ser	Asp	Glu	Gln	Ala
	1075					1080						1085			
Gln	Ala	Leu	Gly	Asn	Gly	Asp	Asn	Ser	Ala	Glu	Leu	Tyr	Leu	Thr	Asp
	1090					1095					1100				
Asn	Ala	Ser	Asn	Ala	Thr	Asp	Gln	Asp	Ala	Ser	Val	Gln	Lys	Pro	Gly
1105				1110						1115					1120
Ser	Thr	Ser	Phe	Asp	Leu	Ile	Val	Asn	Gly	Gly	Gly	Ile	Pro	Asp	Lys
			1125						1130					1135	
Ile	Ser	Ser	Thr	Thr	Thr	Gly	Tyr	Glu	Ala	Asn	Thr	Gln	Gly	Gly	Gly
			1140				1145						1150		

-continued

---

Thr Tyr Thr Phe Ser Gly Thr Tyr Pro Ala Ala Val Asp Gly Thr Tyr  
 1155 1160 1165

Thr Asp Ala Gln Gly Lys Lys His Asp Leu His Thr Thr Tyr Asp Ala  
 1170 1175 1180

Ala Thr Asn Ser Phe Thr Ala Ser Met Ala Val Thr Asn Ala Asp Tyr  
 1185 1190 1195 1200

Ala Ala Gln Val Asp Leu Tyr Ala Asp Lys Ala His Thr Arg Leu Leu  
 1205 1210 1215

Lys His Phe Asp Thr Lys Val Arg Leu Thr Ala Pro Thr Phe Thr Asp  
 1220 1225 1230

Leu Lys Phe Asn Asn Gly Ser Asp Gln Thr Ser Glu Ala Thr Ile Lys  
 1235 1240 1245

Val Thr Gly Thr Val Ser Ala Asp Thr Lys Thr Val Asn Val Gly Asp  
 1250 1255 1260

Thr Val Ala Ala Leu Asp Ala Gln His His Phe Ser Val Asp Val Pro  
 1265 1270 1275 1280

Val Asn Tyr Gly Asp Asn Thr Ile Lys Val Thr Ala Thr Asp Glu Asp  
 1285 1290 1295

Gly Asn Thr Thr Thr Glu Gln Lys Thr Ile Thr Ser Ser Tyr Asp Pro  
 1300 1305 1310

Asp Val Leu Lys Asn Ala Val Thr Phe Asp Gln Gly Val Thr Phe Gly  
 1315 1320 1325

Ala Asn Glu Phe Asn Ala Thr Ser Ser Lys Phe Tyr Asp Pro Lys Thr  
 1330 1335 1340

Gly Ile Ala Thr Ile Thr Gly Lys Val Lys His Pro Thr Thr Thr Leu  
 1345 1350 1355 1360

Gln Val Asp Gly Lys Gln Ile Pro Ile Lys Asp Asp Leu Thr Phe Ser  
 1365 1370 1375

Phe Thr Leu Asp Leu Gly Thr Leu Gly Gln Lys Pro Phe Gly Val Val  
 1380 1385 1390

Val Gly Asp Thr Thr Gln Asn Lys Thr Phe Gln Glu Ala Leu Thr Phe  
 1395 1400 1405

Ile Leu Asp Ala Val Ala Pro Thr Leu Ser Leu Asp Ser Ser Thr Asp  
 1410 1415 1420

Ala Pro Val Tyr Thr Asn Asp Pro Asn Phe Gln Ile Thr Gly Thr Ala  
 1425 1430 1435 1440

Thr Asp Asn Ala Gln Tyr Leu Ser Leu Ala Ile Asn Gly Ser His Val  
 1445 1450 1455

Ala Ser Gln Tyr Ala Asp Ile Asn Ile Asn Ser Gly Lys Pro Gly His  
 1460 1465 1470

Met Ala Ile Asp Gln Pro Val Lys Leu Leu Glu Gly Lys Asn Val Leu  
 1475 1480 1485

Thr Val Ala Val Thr Asp Ser Glu Asn Asn Thr Thr Thr Lys Lys Ile  
 1490 1495 1500

Thr Val Tyr Tyr Glu Pro Lys Lys Thr Leu Ala Ala Pro Thr Val Thr  
 1505 1510 1515 1520

Pro Ser Thr Thr Glu Pro Ala Lys Thr Val Thr Leu Thr Ala Asn Ala  
 1525 1530 1535

Ala Ala Thr Gly Glu Thr Val Gln Tyr Ser Ala Asp Gly Gly Lys Thr  
 1540 1545 1550

Tyr Gln Asn Val Pro Ala Ala Gly Val Thr Val Thr Ala Asn Gly Thr  
 1555 1560 1565

Phe Lys Phe Lys Ser Thr Asp Leu Tyr Gly Asn Glu Ser Pro Ala Val

-continued

---

1570	1575	1580
Asp Tyr Val Val Thr Asn Ile Lys Thr Asp Asp Pro Ala Gln Leu Gln 1585	1590	1595 1600
Thr Ala Lys Gln Ala Leu Thr Asn Leu Ile Ala Ser Ala Lys Thr Leu 1605	1610	1615
Ser Ala Ser Gly Lys Tyr Asp Asp Ala Thr Thr Thr Ala Leu Ala Ala 1620	1625	1630
Ala Thr Gln Lys Ala Gln Thr Ala Leu Asp Gln Thr Asp Ala Ser Val 1635	1640	1645
Asp Ser Leu Thr Gly Ala Asn Arg Asp Leu Gln Thr Ala Ile Asn Gln 1650	1655	1660
Leu Ala Ala Lys Leu Pro Ala Asp Lys Lys Thr Ser Leu Leu Asn Gln 1665	1670	1675 1680
Leu Gln Ser Val Lys Ala Ala Leu Gly Thr Asp Leu Gly Asn Gln Thr 1685	1690	1695
Asp Pro Ser Thr Gly Lys Thr Phe Thr Ala Ala Leu Asp Asp Leu Val 1700	1705	1710
Ala Gln Ala Gln Ala Gly Thr Gln Thr Ala Asp Gln Leu Gln Ala Thr 1715	1720	1725
Leu Ala Lys Val Leu Asp Ala Val Leu Ala Lys Leu Ala Glu Gly Ile 1730	1735	1740
Lys Ala Ala Thr Pro Ala Glu Val Gly Asn Ala Lys Asp Ala Ala Thr 1745	1750	1755 1760
Gly Lys Thr Trp Tyr Ala Asp Ile Ala Asp Thr Leu Thr Ser Gly Gln 1765	1770	1775
Ala Ser Ala Asp Ala Ser Asp Lys Leu Ala His Leu Gln Ala Leu Gln 1780	1785	1790
Ser Leu Lys Thr Lys Val Ala Ala Ala Val Glu Ala Ala Lys Thr Ala 1795	1800	1805
Gly Lys Gly Asp Asp Thr Ser Gly Thr Ser Asp Lys Gly Gly Gly Gln 1810	1815	1820
Gly Thr Pro Ala Pro Ala Pro Gly Asp Thr Gly Lys Asn Lys Gly Asp 1825	1830	1835 1840
Glu Gly Ser Gln Pro Ser Ser Gly Gly Asn Ile Pro Thr Lys Pro Ala 1845	1850	1855
Thr Thr Thr Ser Thr Ser Thr Asp Asp Thr Thr Asp Arg Asn Gly Gln 1860	1865	1870
His Thr Ser Gly Lys Gly Ala Leu Pro Lys Thr Ala Glu Thr Thr Glu 1875	1880	1885
Arg Pro Ala Phe Gly Phe Leu Gly Val Ile Val Val Ser Leu Met Gly 1890	1895	1900
Val Leu Gly Leu Lys Arg Lys Gln Arg Glu Glu 1905	1910	1915

&lt;210&gt; SEQ ID NO 22

&lt;211&gt; LENGTH: 1627

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Lactobacillus acidophilus

&lt;400&gt; SEQUENCE: 22

Met Arg Asn Lys Lys Val Gly Ser Val Thr Thr Asp Tyr Ser Tyr Leu 1	5	10	15
--	---	----	----

Asn Gln Ser Arg Asn His Leu Asn Leu Val Thr Gly Lys Glu Asn Asp 20	25	30
---	----	----

Ser Lys Leu Lys Ile Trp Arg Lys Asn Phe Ala Thr Ala Ala Ile Ile
---

-continued

35			40			45									
Ala	Leu	Ala	Ser	Gly	Thr	Thr	Met	Leu	Phe	Ser	Ala	His	Ser	Val	Lys
	50						55				60				
Ala	Asp	Glu	Val	Asp	Asp	Ile	Thr	Val	Gln	Asn	Asp	Lys	Gln	Val	Asn
65					70					75					80
Thr	Thr	Ile	Val	Gln	Asn	Asn	Lys	Asp	Gln	Gln	Ser	Ser	Asp	Thr	Gln
				85					90					95	
Gln	Asn	Val	Asn	Glu	Asn	Arg	Ala	Ser	Ser	Gln	Gln	Ala	Ile	Arg	Arg
			100					105					110		
Pro	Gly	Thr	Gly	Asn	Lys	Leu	Thr	Asp	Gln	Trp	Pro	Asp	Asn	Tyr	Gln
		115					120					125			
Ser	Asp	Gln	Gln	Asn	Asn	Ser	Ser	Gln	Ala	Glu	Thr	Thr	Lys	Ile	Ser
	130					135					140				
Thr	Thr	Gly	Tyr	Ser	Asn	Gln	Thr	Glu	Gln	Gln	Ser	Asn	Asn	Thr	Val
145					150					155					160
Pro	Ser	Thr	Val	Ala	Ser	Ser	Thr	Val	Tyr	Lys	Glu	Ser	Ser	Asp	Asp
				165					170					175	
Gln	Ala	Gly	Gln	Lys	Asp	Thr	Asn	Gly	Val	Glu	Leu	Pro	Ala	Asn	Asn
			180					185						190	
Gln	Asp	His	Ile	Lys	Gly	Asn	Val	Gln	Asp	Ala	Trp	Asp	Gln	Gly	Tyr
		195					200					205			
Lys	Gly	Gln	His	Thr	Val	Val	Ala	Val	Ile	Asp	Ser	Gly	Val	Asp	Thr
	210					215					220				
Ser	His	Lys	Asp	Phe	Gln	Thr	Met	Pro	Glu	Asn	Pro	Lys	Leu	Ser	Gln
225					230					235					240
Ala	Glu	Ile	Glu	Ala	Leu	Ile	Ala	Lys	Leu	Gly	Tyr	Gly	Thr	Tyr	Ile
				245					250					255	
Asn	Ser	Lys	Phe	Pro	Phe	Val	Tyr	Asn	Ala	Val	Asp	His	Glu	Asn	Gln
			260					265					270		
Ser	Met	Lys	Gly	Pro	Asp	Gly	Glu	Pro	His	Gly	Gln	His	Val	Ser	Gly
		275					280					285			
Ile	Ile	Ala	Ala	Asp	Gly	Gln	Pro	Asn	Gly	Asp	Gln	Glu	Tyr	Val	Val
	290					295					300				
Gly	Val	Ala	Pro	Glu	Ala	Gln	Leu	Met	His	Phe	Lys	Val	Phe	Gly	Asp
305					310					315					320
Asn	Ala	Thr	Ser	Leu	Asp	Leu	Ala	Gln	Glu	Ile	Tyr	Asp	Ala	Thr	Asn
				325					330					335	
Leu	Gly	Ala	Asp	Val	Ile	Gln	Met	Ser	Leu	Gly	Gly	Gly	Val	Ala	Ala
			340					345					350		
Ala	Asp	Leu	Asn	Val	Ala	Asp	Gln	Arg	Ala	Val	Gln	Tyr	Ala	Ile	Asp
		355					360					365			
His	Gly	Val	Ile	Val	Ser	Ile	Ser	Ala	Ser	Asn	Asn	Gly	Asn	Ala	Ala
	370					375					380				
Ser	Ile	Gln	Asn	Pro	Ser	Asn	Val	Thr	Asp	Leu	Asp	Asn	Tyr	Glu	Ala
385						390				395					400
Gly	Thr	His	Val	Gly	Asn	Tyr	Glu	Pro	Phe	Ser	Ser	Ser	Thr	Val	Ala
				405					410					415	
Asp	Pro	Gly	Ala	Ala	Arg	Gly	Ala	Ile	Thr	Gly	Ala	Ala	Glu	Thr	Ser
			420					425					430		
Gly	Leu	Gly	Asp	Lys	Ser	Asp	Met	Ala	Thr	Phe	Thr	Ser	Trp	Gly	Pro
		435					440					445			
Leu	Pro	Asp	Phe	Thr	Leu	Lys	Pro	Asp	Val	Ser	Ala	Pro	Gly	Ser	Asn
	450					455					460				



-continued

Val	Ile	Ser	Leu	Ala	Asn	Asp	Asn	Gly	Tyr	Thr	Thr	Met	Ser	Gly	Thr	465	470	475	480
Ser	Met	Ala	Gly	Pro	Phe	Ile	Ala	Gly	Ala	Ala	Ala	Leu	Val	Arg	Gln	485	490	495	
Arg	Leu	Gln	Gln	Thr	Asn	Pro	Glu	Leu	Lys	Gly	Ala	Asp	Leu	Val	Ala	500	505	510	
Ala	Val	Lys	Ala	Leu	Leu	Met	Asn	Thr	Ala	Asp	Pro	Gln	Ile	Gln	Gln	515	520	525	
Gly	Phe	Thr	Thr	Ile	Val	Ser	Pro	Arg	Arg	Gln	Gly	Ala	Gly	Gln	Ile	530	535	540	
Asn	Val	Gly	Ala	Ala	Thr	Lys	Ala	Pro	Val	Tyr	Ile	Leu	Ala	Asn	Asp	545	550	555	560
Gly	Thr	Gly	Ser	Val	Ser	Leu	Arg	Asn	Ile	Lys	Glu	Thr	Thr	Asn	Phe	565	570	575	
Glu	Leu	Thr	Phe	His	Asn	Leu	Thr	Asp	Asn	Thr	Glu	Thr	Tyr	Thr	Phe	580	585	590	
Asp	Asp	Leu	Gly	Gly	Gly	Phe	Thr	Glu	Val	Arg	Asp	Thr	Asp	Thr	Gly	595	600	605	
Leu	Phe	His	Asp	Val	Gln	Leu	Ala	Gly	Ala	Arg	Val	Thr	Gly	Pro	Asn	610	615	620	
Thr	Ile	Thr	Val	Asn	Pro	Lys	Glu	Thr	Lys	Lys	Ile	Val	Phe	Thr	Leu	625	630	635	640
Asn	Leu	Thr	Gly	Leu	Lys	Gln	Asn	Gln	Leu	Val	Glu	Gly	Tyr	Leu	Asn	645	650	655	
Phe	Thr	Asn	Ser	Lys	Asp	Lys	Leu	Ser	Leu	Ser	Val	Pro	Tyr	Leu	Gly	660	665	670	
Tyr	Tyr	Gly	Asp	Met	Thr	Ser	Glu	Asp	Val	Phe	Asp	Lys	Lys	Ala	Asn	675	680	685	
Glu	Asp	Lys	Pro	Asp	Ile	Lys	Gly	Asn	Arg	Leu	Thr	Asn	Glu	Asp	Asn	690	695	700	
Tyr	Pro	Arg	Gly	Ile	Ala	Asp	Glu	Glu	Ser	Leu	Lys	Glu	Leu	Val	Asn	705	710	715	720
Ile	Glu	Gly	Asn	Tyr	Asn	Trp	Gln	Glu	Val	Ala	Lys	Leu	Tyr	Glu	Ser	725	730	735	
Gly	Lys	Val	Ala	Phe	Ser	Pro	Asn	Gly	Asp	Asn	Lys	Ser	Asp	Leu	Ile	740	745	750	
Met	Pro	Tyr	Val	Tyr	Leu	Lys	Gln	Asn	Leu	Gln	Asp	Leu	Lys	Val	Glu	755	760	765	
Ile	Leu	Asp	Ala	Lys	Gly	Asn	Val	Val	Arg	Val	Leu	Ala	Asp	Ala	His	770	775	780	
Gly	Val	Gln	Lys	Ser	Tyr	Asn	Glu	Asp	Gly	Thr	Gly	Thr	Val	Asp	Ala	785	790	795	800
Leu	Ile	Ser	Val	Asp	Ser	Gly	Lys	Phe	Asn	Trp	Asp	Gly	Lys	Val	Tyr	805	810	815	
Asn	Tyr	Lys	Thr	Gly	Lys	Met	Glu	Val	Ala	Pro	Asp	Gly	Gln	Tyr	Thr	820	825	830	
Tyr	Arg	Phe	Val	Ala	Thr	Leu	Tyr	Asn	Asp	Gly	Pro	His	Lys	Val	Gln	835	840	845	
Thr	Asn	Asp	Thr	Ser	Val	Ile	Ile	Asp	Thr	Thr	Ala	Pro	Ile	Leu	Lys	850	855	860	
Asp	Val	Glu	Tyr	Asp	Val	Thr	Thr	Lys	Thr	Ile	Thr	Gly	Thr	Tyr	Ser	865	870	875	880
Asp	Ala	Gly	Ala	Gly	Phe	Thr	Asp	Tyr	Ser	Tyr	Ala	Thr	Val	Thr	Ile	885	890	895	

-continued

---

Asn Asp Arg Val Phe Gly Phe Lys Leu Asn Asp Asn Asp Asn Ser Thr  
 900 905 910  
 Phe Asp Asn Thr Asp Lys Thr Ile Gly His Phe Ser Phe Ala Leu Thr  
 915 920 925  
 Pro Leu Glu Gln Gln Ala Leu Thr Ala Ala His Asn Lys Val Ser Val  
 930 935 940  
 Cys Leu Ser Asp Val Ala Asp Asn Thr Ala Val Lys Thr Leu Asp Val  
 945 950 955 960  
 Ala Ser Val Gly Asp Gly Asn Lys Ile Ala Ile Trp Asn Ala Val Asn  
 965 970 975  
 Gly Val Pro Phe Asn Ser Asn Ser Gln Asp Tyr Ser Asp Lys Asn Asn  
 980 985 990  
 Ser Tyr Leu Leu Arg Gly Ser Ala Thr Glu Asn Phe Tyr Val Asn Gly  
 995 1000 1005  
 Lys Leu Val Gln Val Ala Pro Asn Gly Glu Phe Val Leu Pro Val Ser  
 1010 1015 1020  
 Leu Asp Glu Gln Asn Leu Val Phe Thr Ser Asp Glu Asn Gly Gln Asn  
 1025 1030 1035 1040  
 Val Leu Arg Gln Phe Thr Thr Tyr Thr Pro Lys Ala Asp Phe Ala Trp  
 1045 1050 1055  
 Gln His Ile Asp Gly Ser Glu Arg Ser Phe Gly Val Ser Val Tyr Ser  
 1060 1065 1070  
 Ile Asp Ala Ala Asp Pro Asn Asp Ala Ile Val Gln Ala Ala Val Pro  
 1075 1080 1085  
 Lys Gly Asn Asn Val Lys Ala Phe Ala Lys Asp Tyr Phe Thr Gly Glu  
 1090 1095 1100  
 Thr Tyr Val Gly Glu Val Lys Asp Gly Val Ala Thr Phe His Ile His  
 1105 1110 1115 1120  
 Thr Ser Ile Asn Pro Asp Pro Gln Thr Gly Ile Asn Arg Arg Ala Leu  
 1125 1130 1135  
 Leu Gln Gly Trp Val Glu Ile Asp Gly Pro Thr Tyr Asn Ala Lys Gln  
 1140 1145 1150  
 Val Thr Asp Pro Thr Ala Ile Ser Asp Arg Asn Tyr Ile Gly Val Tyr  
 1155 1160 1165  
 Tyr Lys Pro Asp Ala Ser Ser His Val Tyr Ser Asn Arg Asp Glu Leu  
 1170 1175 1180  
 Gly Val Asp Asp Phe Thr Asp Glu Gln Ala Asp Val Ser Asp Phe Gly  
 1185 1190 1195 1200  
 Pro Ser Lys Phe Leu Tyr Pro Gly His Asn Ala Pro Ser Asp Gly Asn  
 1205 1210 1215  
 Ala Asn Ile Ser Phe Asp Tyr Val Asn Asp Asn Asn Ile Ser Thr Phe  
 1220 1225 1230  
 Gly Gln Glu Ala Val Lys Ala Gly Tyr Tyr Asp Pro Ile Ala Lys Val  
 1235 1240 1245  
 Phe Thr Ile Thr Gly His Val Asp Lys Asp Val Val Ser Leu Val Ala  
 1250 1255 1260  
 Leu Gln Asp Asn Pro Asn Glu Asp Ala Pro Glu Asn Arg Val Ala Ile  
 1265 1270 1275 1280  
 Asp Lys Asp Gly Asn Phe Ile Ile Lys Phe His Met Asp Asp Pro Ser  
 1285 1290 1295  
 Thr Arg Gln Leu Thr Tyr Ile Tyr Lys Val Lys Asp Ser Ser Thr Asp  
 1300 1305 1310  
 Lys Ile Asp Thr Val Lys Gly Ser Ile Thr Leu Ile Leu Asp Thr Val

-continued

1315	1320	1325
Leu Pro Thr Leu His Val Asp Gln Leu Asn Gly Ala Asp Asn Leu Thr 1330 1335 1340		
Ile Thr Thr Asn Asn Pro Thr Phe Lys Ile Ser Gly Asn Ala Asn Asp 1345 1350 1355 1360		
Asp Leu Asp Asp Tyr Ser Val Tyr Ile Asn Gly Asp Asn Val Phe Thr 1365 1370 1375		
Gln Phe Asn Gly Ser Ser Phe Asn Tyr Ile Pro Gly Met Tyr Gly Asp 1380 1385 1390		
Pro Asn Gln Lys Thr Pro Asn Leu Tyr Gly Gly Tyr Asp Phe Glu Gln 1395 1400 1405		
Glu Val Asn Leu Asp Asp Glu Asn Gly Lys Pro Thr Thr His Ile Phe 1410 1415 1420		
Asn Ile Glu Leu Ile Asp Gln Val Gly Asn Lys Val Phe Lys Thr Leu 1425 1430 1435 1440		
Thr Val Asn Tyr Asp Pro Asn Ala Thr Asn Ser Glu Asp Pro Ser Asn 1445 1450 1455		
Gly Thr Gly Asp Ser Gly Ile Glu Val Val Pro Thr Val Pro Arg Lys 1460 1465 1470		
Val Gln Pro Leu Ser Asp Asp Asn Ser Thr Asn Ile Asn Asp Lys Gln 1475 1480 1485		
Thr Leu Ser Thr Glu Leu Thr Ile Thr Leu Pro Arg Asn Ile Phe Ala 1490 1495 1500		
Phe Asp Tyr Gln Gly Lys Val Ala Arg Lys His Gly Lys Asp Ile Ile 1505 1510 1515 1520		
Leu Lys Lys Gly Val Val Leu Tyr Asn Pro Lys Glu Val Asn Ile Arg 1525 1530 1535		
Lys His Lys Tyr Tyr Lys Val Ser Lys Asn Val Tyr Ile Lys Val Thr 1540 1545 1550		
Ser Thr Arg Val Asn Lys Lys Leu Lys Arg Leu Ile Leu Ile Lys Asn 1555 1560 1565		
Ser Tyr Val Tyr Asn Leu Asn Gly Lys Ala Asn Lys Val His Asn Lys 1570 1575 1580		
Arg Val Leu Leu Lys Arg Gly Leu Ala Val Asp Val Leu His Gly Gly 1585 1590 1595 1600		
Lys Ile Thr Lys Val Gly Lys Tyr Asp Cys Tyr Gln Ile Gly Ile Asn 1605 1610 1615		
Gln Tyr Ile Lys Val Ala Asn Thr Ala Leu Lys 1620 1625		

&lt;210&gt; SEQ ID NO 23

&lt;211&gt; LENGTH: 1643

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Streptococcus thermophilus

&lt;400&gt; SEQUENCE: 23

Met Pro Thr Ile Leu Cys Phe Asn Ile Phe Ile Gly Phe Ala Asn Asn 1 5 10 15
Glu Gly Glu Lys Leu Gly Gly Lys Val Met Lys Lys Lys Glu Thr Phe 20 25 30
Ser Leu Arg Lys Tyr Lys Ile Gly Thr Val Ser Val Leu Leu Gly Ala 35 40 45
Val Phe Leu Phe Ala Gly Ala Pro Ser Val Ala Ala Asp Glu Leu Thr 50 55 60
Ser Leu Val Glu Thr Lys Val Glu Ala Thr Val Pro Asp Ala Ile Val

-continued

65	70	75	80
Ser Glu Ser Ala Ser Glu Ser Pro Val Ala Glu Glu Leu Val Asp Thr	85	90	95
Ser Val Glu Ala Thr Ser Thr Asp Val Thr Thr Thr Asp Asn Glu Glu	100	105	110
Glu Thr Leu Gly Ser Glu Ser Pro Val Val Glu Glu Leu Val Asp Thr	115	120	125
Ser Val Glu Ala Thr Pro Thr Asp Val Thr Thr Thr Asp Asn Val Glu	130	135	140
Glu Thr Leu Gly Ser Glu Ala Leu Glu Asn Ile Thr Asn Thr Glu Val	145	150	155
Glu Ala Thr Gln Pro Ala Val Glu Thr Pro Ala Ile Ser Glu Lys Lys	165	170	175
Val Glu Glu Glu Glu Lys Leu Ser Val Ala Asp Glu Thr Thr Ala Ile	180	185	190
Thr Asn Gln Glu Glu Ala Lys Pro Gln Asn Ile Asp Ser Asn Thr Ile	195	200	205
Ile Thr Val Pro Lys Val Trp Asp Ser Gly Tyr Lys Gly Glu Gly Thr	210	215	220
Val Val Ala Ile Ile Asp Ser Gly Leu Asp Val Asp His Asp Val Leu	225	230	235
His Ile Ser Asp Leu Ser Thr Ala Lys Tyr Lys Ser Glu Lys Glu Ile	245	250	255
Glu Ala Ala Lys Glu Val Ala Gly Ile Ser Tyr Gly Glu Trp Phe Asn	260	265	270
Asp Lys Val Val Phe Gly Tyr Asn Tyr Val Asp Val Asn Thr Val Leu	275	280	285
Lys Glu Glu Asp Lys Arg Ser His Gly Met His Val Thr Ser Ile Ala	290	295	300
Thr Gly Asn Pro Thr Gln Pro Val Ala Gly Gln Leu Met Tyr Gly Val	305	310	315
Ala Pro Glu Ala Gln Val Met Phe Met Arg Val Phe Ser Asp Leu Lys	325	330	335
Ala Thr Thr Gly Ala Ala Leu Tyr Val Lys Ala Ile Glu Asp Ala Val	340	345	350
Lys Leu Gly Ala Asp Ser Ile Asn Leu Ser Leu Gly Gly Ala Asn Gly	355	360	365
Ser Val Val Asn Met Asn Glu Asn Val Thr Ala Ala Ile Glu Ala Ala	370	375	380
Arg Arg Ala Gly Val Ser Val Val Ile Ala Ala Gly Asn Asp Gly Thr	385	390	395
Phe Gly Ser Gly His Ser Asn Pro Ser Ala Asp Tyr Pro Asp Tyr Gly	405	410	415
Leu Val Gly Ala Pro Ser Thr Ala Arg Asp Ala Ile Ser Val Ala Ser	420	425	430
Tyr Asn Asn Thr Thr Val Gly Ser Lys Val Ile Asn Ile Ile Gly Leu	435	440	445
Glu Asn Asn Ala Asp Leu Asn Tyr Gly Lys Ser Ser Phe Asp Asn Pro	450	455	460
Glu Lys Ser Pro Val Pro Phe Glu Ile Gly Lys Glu Tyr Glu Tyr Val	465	470	475
Tyr Ala Gly Ile Gly Gln Ala Ser Asp Phe Asp Gly Leu Asp Leu Thr	485	490	495

-continued

Gly	Lys	Leu	Ala	Leu	Ile	Lys	Arg	Gly	Thr	Ile	Ser	Phe	Ser	Glu	Lys
		500						505					510		
Ile	Ala	Asn	Ala	Thr	Ala	Ala	Gly	Ala	Val	Gly	Val	Val	Ile	Phe	Asn
		515					520					525			
Ser	Arg	Pro	Asp	Glu	Ala	Asn	Val	Ser	Met	Gln	Leu	Asp	Asp	Thr	Ala
	530					535					540				
Ile	Ala	Ile	Pro	Ser	Val	Phe	Ile	Pro	Leu	Glu	Phe	Gly	Glu	Ala	Leu
545					550					555					560
Ala	Ala	Asn	Ser	Tyr	Lys	Ile	Ala	Phe	Asn	Asn	Glu	Thr	Asp	Ile	Arg
				565					570					575	
Pro	Asn	Pro	Glu	Ala	Gly	Leu	Leu	Ser	Asp	Phe	Ser	Ser	Trp	Gly	Leu
			580					585					590		
Ser	Ala	Asp	Gly	Glu	Leu	Lys	Pro	Asp	Leu	Ala	Ala	Pro	Gly	Gly	Ala
		595					600					605			
Ile	Tyr	Ala	Ala	Ile	Asn	Asp	Asn	Asp	Tyr	Ala	Asn	Met	Gln	Gly	Thr
	610					615					620				
Ser	Met	Ala	Ser	Pro	His	Val	Ala	Gly	Ala	Ala	Val	Leu	Val	Lys	Gln
625					630					635					640
Tyr	Leu	Gln	Ala	Thr	Tyr	Pro	Thr	Lys	Ser	Pro	Gln	Glu	Ile	Glu	Ala
				645					650					655	
Leu	Val	Lys	His	Leu	Leu	Met	Ser	Thr	Ala	Lys	Ala	His	Val	Asn	Lys
			660					665					670		
Glu	Thr	Thr	Ala	Tyr	Thr	Ser	Pro	Arg	Gln	Gln	Gly	Ala	Gly	Ile	Ile
			675				680					685			
Asp	Thr	Ala	Ala	Ala	Ile	Ser	Thr	Gly	Leu	Tyr	Leu	Thr	Gly	Glu	Asp
	690					695					700				
Gly	Tyr	Gly	Ser	Ile	Thr	Leu	Gly	Asn	Val	Glu	Asp	Thr	Phe	Ser	Phe
705					710					715					720
Thr	Val	Thr	Leu	His	Asn	Ile	Thr	Asn	Glu	Asp	Lys	Thr	Leu	Asn	Tyr
				725					730					735	
Ser	Thr	Gln	Leu	Thr	Thr	Asp	Thr	Val	Gln	Asn	Gly	Leu	Ile	Thr	Leu
			740					745					750		
Ala	Pro	Arg	Leu	Leu	Ala	Glu	Ile	Pro	Gly	Gly	Lys	Val	Thr	Val	Gln
		755					760					765			
Ala	Asn	Ser	Ser	Thr	Thr	Val	Thr	Ile	Asn	Val	Asp	Ala	Ser	Ser	Phe
	770					775					780				
Ala	Glu	Glu	Leu	Thr	Gly	Leu	Met	Lys	Asn	Gly	Tyr	Tyr	Leu	Glu	Gly
785					790					795					800
Phe	Val	Arg	Phe	Thr	Asp	Val	Ala	Asp	Gly	Gly	Asp	Ile	Val	Ser	Ile
			805						810					815	
Pro	Tyr	Ile	Gly	Phe	Arg	Gly	Glu	Phe	Gln	Asn	Leu	Ala	Val	Leu	Glu
			820					825					830		
Glu	Pro	Ile	Tyr	Asn	Leu	Ile	Ala	Asp	Gly	Lys	Gly	Gly	Phe	Tyr	Phe
		835					840					845			
Glu	Pro	Val	Thr	Ala	Gln	Pro	Asp	Ser	Val	Asp	Ile	Ser	His	His	Tyr
	850					855					860				
Thr	Gly	Leu	Val	Thr	Gly	Ser	Thr	Glu	Leu	Ile	Tyr	Ser	Thr	Asp	Lys
865					870						875				880
Arg	Ser	Asp	Phe	Ala	Ile	Lys	Lys	Thr	Leu	Gly	Thr	Phe	Lys	Asn	Glu
			885						890					895	
Ala	Gly	Tyr	Phe	Val	Leu	Glu	Leu	Asp	Glu	Ser	Gly	Lys	Pro	His	Leu
			900					905					910		
Ala	Ile	Ser	Pro	Asn	Gly	Asp	Asp	Asn	Gln	Asp	Ser	Leu	Ala	Phe	Lys
		915					920						925		

-continued

---

Gly Val Phe Leu Arg Asn Tyr Thr Asp Leu Val Ala Ser Val Tyr Ala  
 930 935 940

Ala Asp Asp Thr Glu Arg Thr Asn Pro Leu Trp Glu Ser Gln Pro Gln  
 945 950 955 960

Ser Gly Asn Lys Asn Phe Tyr Ser Gly Asp Pro Lys Asn Pro Lys Ser  
 965 970 975

Ser Ile Ile Tyr Pro Thr Glu Trp Asn Gly Thr Asp Ser Glu Gly Asn  
 980 985 990

Ala Leu Ala Asp Gly Lys Tyr Gln Tyr Val Leu Thr Tyr Ser Ser Glu  
 995 1000 1005

Val Pro Gly Ala Ala Val Gln Thr Met Ile Phe Asp Val Ile Ile Asp  
 1010 1015 1020

Arg Glu Ser Pro Val Ile Thr Thr Ala Thr Tyr Asp Glu Thr Asn Phe  
 1025 1030 1035 1040

Thr Phe Asn Pro Arg Pro Ala Ile Glu Lys Gly Glu Ser Gly Leu Tyr  
 1045 1050 1055

Arg Glu Gln Val Phe Tyr Leu Val Ala Asp Ala Ser Gly Val Thr Thr  
 1060 1065 1070

Ile Pro Ser Leu Leu Glu Asn Gly Asp Val Thr Val Ser Asp Asn Lys  
 1075 1080 1085

Val Phe Val Ala Gln Asn Asp Asp Gly Ser Phe Thr Leu Pro Leu Asp  
 1090 1095 1100

Leu Ala Asp Ile Ser Lys Phe Tyr Tyr Thr Val Glu Asp Tyr Ala Gly  
 1105 1110 1115 1120

Asn Ile Ser Tyr Glu Lys Val Glu Asn Leu Ile Ser Ile Gly Asn Glu  
 1125 1130 1135

Lys Gly Leu Val Thr Val Asn Ile Leu Asp Lys Asp Thr Asn Ser Pro  
 1140 1145 1150

Val Pro Ile Leu Phe Ser Tyr Ser Val Thr Asp Glu Thr Gly Lys Ile  
 1155 1160 1165

Val Ala Glu Leu Pro Arg Tyr Ala Gly Asp Thr Ser Val Leu Lys Leu  
 1170 1175 1180

Pro Phe Gly Thr Tyr Thr Phe Asp Leu Phe Leu Tyr Asp Thr Glu Trp  
 1185 1190 1195 1200

Ser Ser Leu Ala Gly Glu Thr Lys Ala Val Val Thr Ile Leu Glu Asp  
 1205 1210 1215

Asn Ser Thr Ala Glu Val Asn Phe Tyr Val Thr Leu Lys Asp Lys Ala  
 1220 1225 1230

Asn Leu Leu Ile Asp Ile Asp Ala Leu Leu Pro Ser Gly Ser Thr Ile  
 1235 1240 1245

Gln Leu Val Thr Ala Asp Gly Gln Ala Ile Gln Leu Pro Asn Ala Lys  
 1250 1255 1260

Tyr Ser Lys Thr Asp Tyr Gly Lys Phe Val Pro Val Gly Thr Tyr Thr  
 1265 1270 1275 1280

Ile Leu Pro Thr Leu Pro Glu Gly Tyr Glu Phe Leu Glu Glu Leu Asp  
 1285 1290 1295

Val Ala Val Leu Ala Asn Gln Ser Asn Val Lys Lys Leu Thr Leu Ile  
 1300 1305 1310

Asn Lys Val Ala Leu Lys Glu Leu Ile Ala Glu Leu Ala Gly Leu Glu  
 1315 1320 1325

Glu Thr Ala Arg Tyr Tyr Asn Ala Ser Pro Glu Leu Gln Thr Ala Tyr  
 1330 1335 1340

Ala Lys Ala Leu Glu Asp Ala Asn Ala Val Tyr Ala Asn Lys His Asn

-continued

1345	1350	1355	1360
Gln Ala Gln Val Asp Ser Ala Leu Ala Ser Leu Val Ala Ala Arg Glu	1365	1370	1375
Gln Leu Asn Gly Gln Ala Thr Asp Lys Glu Lys Leu Ile Ala Glu Val	1380	1385	1390
Ser Asn Tyr Thr Pro Thr Gln Ala Asn Phe Ile Tyr Tyr Asn Ala Glu	1395	1400	1405
Asn Thr Lys Gln Ile Ala Tyr Asp Thr Ala Val Arg Ser Ala Gln Leu	1410	1415	1420
Val Leu Asn Gln Glu Asn Val Thr Gln Ala Val Val Asn Gln Ala Leu	1425	1430	1435
Ala Asp Leu Leu Ala Ala Lys Ala Asn Leu Asp Gly Gln Lys Thr Asp	1445	1450	1455
Ile Ser Ala Leu Arg Ser Ala Val Ser Val Ser Ser Val Leu Lys Ala	1460	1465	1470
Thr Asp Ala Lys Tyr Leu Asn Ala Ser Glu Asn Val Lys Gln Ala Tyr	1475	1480	1485
Asp Gln Ala Val Glu Ala Ala Lys Ala Ile Leu Val Asp Glu Ser Ala	1490	1495	1500
Ser Gln Ala Ser Val Asp Gln Ala Leu Ala Val Leu Thr Ser Ala Gln	1505	1510	1515
Ala Glu Leu Asp Gly Val Ala Thr Ser Thr Asn Asp Ala Lys Glu Pro	1525	1530	1535
Ala Asn Thr Ala Thr Asp Lys Lys Asp Glu Gly Thr Val Thr Pro Pro	1540	1545	1550
Pro Ile Asp Ser Glu Ile Val Asp Val Gln Ala Pro Pro Val Lys Asp	1555	1560	1565
Thr Gly Asn Ser Glu His Val Pro Ile Gly Gln Lys Pro Asn Pro Gln	1570	1575	1580
Pro Thr Leu Pro Arg Pro Val Thr Leu Gln Ala Ser Leu Ser Ser Pro	1585	1590	1595
Asn Gln Glu Lys Gln Val Thr Gln Leu Pro Asn Thr Gly Glu Asn Asp	1605	1610	1615
Thr Lys Tyr Tyr Leu Val Pro Gly Val Ile Ile Gly Leu Gly Thr Leu	1620	1625	1630
Leu Val Ser Ile Arg Arg His Lys Glu Glu Val	1635	1640	

&lt;210&gt; SEQ ID NO 24

&lt;211&gt; LENGTH: 2179

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Lactobacillus johnsonii

&lt;400&gt; SEQUENCE: 24

Met Lys Lys Lys Arg Glu Lys Tyr Thr Trp Leu Leu Leu Ser Thr Ala	1	5	10	15
Leu Ile Thr Ser Gly Gln Ile Leu Gly Gly Gly Glu Gln Ile Ile Lys	20	25	30	
Ala Ser Val Glu Ser Gln Thr Asn Ser Val Lys Lys Ser Lys Thr Ala	35	40	45	
Val Glu His Ser Thr Thr Ala Leu Ser Arg Gln Ala Val Glu Ala Gln	50	55	60	
Leu Ala Ala Gln Gly Val Asn Phe Glu Arg Leu Thr Pro Glu Glu Gln	65	70	75	80
Gln Glu Val Tyr Val Asp Val Ile Val Gln Leu Glu Ala Leu Pro Ala				

-continued

85				90				95							
Ser	Glu	Asn	Gly	Ser	Ile	Asp	Ser	Gln	Thr	Ala	Ser	Arg	Ala	Glu	Ile
		100						105					110		
Glu	Gln	Ala	Ser	Asn	Lys	Val	Ile	Ala	Ala	Gln	Ser	Gly	Ile	Lys	Asp
		115					120					125			
Glu	Val	Gln	Lys	Ile	Thr	Asn	Gln	Ala	Ile	Asp	Lys	Ser	Tyr	Gly	Tyr
	130					135					140				
Val	Val	Asn	Gly	Phe	Ala	Thr	Lys	Ala	Lys	Val	Gly	Asp	Ile	Lys	Lys
145					150					155					160
Leu	Arg	Glu	Ile	Lys	Gly	Val	Lys	Ser	Val	Thr	Leu	Ala	Lys	Val	Tyr
			165						170				175		
Phe	Ala	Ala	Asp	Thr	Ser	Ala	Asn	Asn	Met	Ala	Asn	Val	Ser	Thr	Val
			180					185					190		
Trp	Ser	Asn	Tyr	Gln	Tyr	Lys	Gly	Glu	Gly	Thr	Val	Val	Ser	Ile	Ile
		195					200					205			
Asp	Thr	Gly	Ile	Asp	Pro	Asn	His	Lys	Asp	Leu	Arg	Leu	Ser	Asp	Glu
	210					215					220				
Ser	Lys	Val	Lys	Leu	Thr	Ala	Lys	Asp	Ile	Asp	Gly	Phe	Thr	Glu	Asn
225					230					235					240
Ser	Gly	Tyr	Gly	Arg	Tyr	Phe	Thr	Ser	Lys	Val	Pro	Phe	Gly	His	Asn
			245						250					255	
Tyr	Ser	Asp	Asn	Asn	Asp	Ile	Ile	Thr	Asp	Asp	Asp	Pro	Lys	Glu	Gln
			260					265					270		
His	Gly	Met	His	Val	Ala	Gly	Ile	Val	Ala	Ala	Asn	Gly	Thr	Gly	Lys
		275					280					285			
Asn	Ser	Ala	Ser	Ser	Val	Val	Gly	Val	Ala	Pro	Glu	Ala	Gln	Leu	Leu
	290					295					300				
Ala	Met	Lys	Ala	Phe	Ser	Asn	Ser	Asp	Ser	Ser	Ser	Thr	Thr	Asp	Ser
305					310					315					320
Thr	Ser	Val	Ile	Gly	Ala	Val	Asp	Asp	Ser	Ala	Lys	Leu	Gly	Ala	Asp
			325					330					335		
Val	Leu	Asn	Met	Ser	Leu	Gly	Ser	Val	Ser	Gly	Glu	Gln	Thr	Glu	Asp
		340						345					350		
Asp	Pro	Glu	Ile	Ala	Ala	Val	Glu	Lys	Ala	Val	Lys	His	Gly	Thr	Ala
		355					360					365			
Ala	Val	Ile	Ser	Gly	Thr	Ser	Arg	Ser	Ala	Thr	Thr	Val	Ala	Ser	Ala
	370					375					380				
Glu	Asn	Thr	Lys	Val	Thr	Thr	Asp	Gly	Met	Thr	Val	Ser	Thr	Ala	Asp
385					390					395					400
Gly	Lys	Lys	Ile	Phe	Gly	Pro	Ser	Val	Thr	Gln	Leu	Ser	Pro	Asn	Thr
			405						410					415	
Ser	His	Asp	Ala	Phe	Asp	Ser	Lys	Lys	Phe	Tyr	Ile	Val	Lys	Asp	Ala
			420					425					430		
Ser	Gly	Lys	Leu	Gly	Met	Gly	Thr	Pro	Ser	Gln	Tyr	Thr	Ala	Asp	Val
		435					440						445		
Lys	Gly	Lys	Val	Ala	Val	Val	Ser	Arg	Gly	Glu	Ile	Thr	Phe	Thr	Asp
	450					455					460				
Lys	Gln	Lys	Tyr	Ala	Gln	Ala	Ala	Gly	Ala	Ala	Gly	Leu	Ile	Ile	Val
465					470					475					480
Asn	Asn	Ala	Gly	Gly	Asn	Thr	Pro	Leu	Thr	Ser	Val	Leu	Tyr	Asn	Glu
			485						490					495	
Gly	Phe	Pro	Thr	Ala	Gly	Leu	Ser	Thr	Asp	Asp	Gly	Asn	Lys	Leu	Val
			500						505				510		



-continued

Ala	Tyr	Val	Glu	Ala	His	Pro	Asp	Glu	Leu	Leu	Arg	Val	Asn	Val	Glu
		515					520					525			
Val	Gln	Pro	Leu	Asn	Asn	Val	Ile	Arg	Glu	Glu	Asp	Leu	Met	Ser	Ser
	530					535					540				
Phe	Thr	Ser	Tyr	Gly	Pro	Val	Ser	Asp	Leu	Ser	Phe	Lys	Pro	Asp	Ile
545					550					555					560
Thr	Ala	Pro	Gly	Gly	Asn	Ile	Trp	Ser	Leu	Gln	Asn	Asn	Asn	Gly	Tyr
				565					570					575	
Ile	Asn	Met	Ser	Gly	Thr	Ser	Met	Ala	Ser	Pro	Phe	Ile	Ala	Gly	Ser
			580					585					590		
Gln	Ala	Leu	Leu	Val	Gln	Ala	Met	Asn	Asp	Lys	Thr	Gly	Lys	Phe	Tyr
		595					600					605			
Glu	Thr	Tyr	Gln	Lys	Met	Ser	Gly	Ser	Glu	Arg	Ala	Ala	Leu	Ile	Lys
	610					615					620				
Asn	Ile	Gln	Met	Asn	Thr	Ala	Asn	Ile	Glu	Val	Asp	Val	Asp	His	Gly
625					630					635					640
Ser	Val	Ile	Glu	Ser	Pro	Arg	Arg	Gln	Gly	Ala	Gly	Leu	Val	Asn	Val
				645					650					655	
Glu	Ala	Ala	Ile	Asn	Ala	Ile	Leu	His	Asn	Pro	Ser	Thr	Val	Ser	Gly
			660					665					670		
Ser	Asn	Gly	Tyr	Pro	Gly	Val	Glu	Leu	Lys	Asp	Phe	Gln	Asp	Arg	Gln
		675					680					685			
His	Gln	Phe	Thr	Ile	Lys	Phe	Thr	Asn	Arg	Thr	Asn	Lys	Asp	Ile	Glu
690						695					700				
Tyr	Gly	Leu	Asn	Glu	Asn	Gly	Lys	Phe	Ser	Asp	Val	Tyr	Thr	Ser	Glu
705					710					715					720
Thr	Asp	Pro	Lys	Thr	Gly	Val	Leu	Phe	Glu	Lys	Lys	Ile	Asp	Gly	Ala
				725					730					735	
Ser	Leu	Thr	Pro	Ser	Glu	Lys	Ile	Val	Val	Pro	Ala	Asn	Ser	Thr	Lys
			740					745					750		
Glu	Val	Thr	Ile	Asn	Leu	Ser	Leu	Pro	Asp	Asn	Phe	Lys	Glu	Asn	Gln
		755					760					765			
Tyr	Val	Glu	Gly	Phe	Met	Ala	Phe	Thr	Gly	Ser	Asp	Asn	Ser	His	Leu
	770					775					780				
Lys	Ile	Pro	Tyr	Met	Gly	Phe	Phe	Gly	Asp	Trp	Ala	Ala	Pro	Ala	Ile
785					790					795					800
Phe	Asp	Gly	Leu	Asn	Gly	Leu	Ala	Phe	Asn	Pro	Gly	Asn	Asn	Asn	Leu
				805					810					815	
Gly	Thr	Ile	Val	Thr	Ala	Gly	Asn	Lys	Asn	Gly	Ala	Val	Gly	Tyr	Ala
			820					825					830		
Gly	Leu	Asn	Gln	Asp	Glu	Asp	Gly	Asn	Tyr	Arg	Val	Asp	Pro	Asp	Ala
		835					840					845			
Ile	Ala	Leu	Ser	Thr	Ala	Asp	Gly	Ala	Ser	Val	Ser	Trp	Val	Arg	Pro
	850					855						860			
Gln	Tyr	Phe	Leu	Phe	Arg	Asn	Ala	Asn	Asp	Val	Lys	Ala	Glu	Ile	Leu
865					870					875					880
Asn	Gln	Asp	Gly	Glu	Val	Ile	Asn	Thr	Leu	Val	Ser	Leu	Ala	His	Val
				885					890					895	
Thr	Lys	Ser	Tyr	Trp	Ala	Ala	Ser	Ser	Gln	Arg	Tyr	Ala	Lys	Phe	Asn
			900					905					910		
Tyr	Ala	Pro	Ala	Trp	Asp	Gly	Thr	Tyr	Phe	Asn	Gln	Gln	Thr	Asn	Lys
		915					920					925			
Thr	Glu	Lys	Val	Pro	Asp	Gly	Thr	Tyr	Thr	Tyr	Arg	Val	Thr	Gly	Thr
	930					935					940				

-continued

---

Val Asp Gly Thr Lys Lys Gln Gln His Tyr Asp Ile Lys Val Lys Val  
 945 950 955 960

Asp Ser Val Lys Pro Glu Val Lys Asn Leu Lys Leu Gly Ser His Lys  
 965 970 975

Asp Gln Thr Gly Lys Val Ser Tyr Val Leu Lys Ala Glu Ala Lys Asp  
 980 985 990

Asn Phe Ser Gly Leu Asn Gly Gln Ala Asn Thr Tyr Val Asn Gly Glu  
 995 1000 1005

Leu Asn Arg Ser Val Ala Tyr Asp Ile Val Gly Ser Ser Ser Asp Gly  
 1010 1015 1020

Tyr Gln Lys Ile Glu Val Pro Leu Ser Asp Glu Gln Val Lys Thr Leu  
 1025 1030 1035 1040

Arg Ala Gly Lys Asn Asp Leu Ala Ile Ala Val Phe Asp Asn Ala Thr  
 1045 1050 1055

Asn Ala Gly Thr Asn Ser Gly Thr Ser Asn Lys Pro Gly Glu Ile Asn  
 1060 1065 1070

Phe Gly Leu Ile Ile Asp Asn Asn Leu Pro Gln Lys Ile Thr Thr Val  
 1075 1080 1085

Ser Asp Gly Tyr Asp Met Thr Asp Asp Ser Tyr Thr Ile Ser Gly Thr  
 1090 1095 1100

Tyr Pro Glu Lys Val Tyr Gly Thr Tyr Thr Asp Lys Asp Gly Lys Glu  
 1105 1110 1115 1120

His Asp Leu Asn Ile Ser Tyr Asp Glu Ala Ser Glu Arg Phe Val Thr  
 1125 1130 1135

Lys Leu Pro Leu Ser Val Ser Asp Tyr Asp Thr Asn Val Lys Phe Tyr  
 1140 1145 1150

Ala Asp Glu Glu His Glu Thr Leu Ile Thr Gln Lys Arg Ile Asn Val  
 1155 1160 1165

Ser Leu Val Pro Pro Lys Leu Glu Ser Leu Lys Val Asp Asp Gln Glu  
 1170 1175 1180

Thr Tyr Thr Gly Asn Glu Glu Ala Lys Leu Ser Gln Thr Ser Glu Asp  
 1185 1190 1195 1200

Thr Val Glu Val Ser Gly Lys Val Ser Asp Asp Thr Asp Lys Val Ala  
 1205 1210 1215

Val Lys Val Ala Gly Lys Thr Tyr Ser Ala Lys Pro Thr Lys Glu His  
 1220 1225 1230

Thr Phe Lys Val Lys Val Pro Val Ser Tyr Gly Glu Asn Thr Met Asn  
 1235 1240 1245

Ile Val Leu Thr Asp Lys Asp Gly Asn Ser Ser Ser Val Lys Gln Ile  
 1250 1255 1260

Val Lys Ser Ser Asp Arg Gly Lys Thr Val Val Ser Ala Lys Asp Val  
 1265 1270 1275 1280

Thr Phe Asp Asn Gly Ile Lys Phe Gly Thr Thr Ser Val Asn Thr Glu  
 1285 1290 1295

Thr Glu Asn Tyr Asp Pro Lys Thr Gly Lys Leu Thr Leu Thr Gly Lys  
 1300 1305 1310

Val Asn Arg Pro Thr Thr Thr Val Arg Ile Gly Asp His Thr Val Lys  
 1315 1320 1325

Val Lys Ala Asp Gly Thr Phe Lys Leu Val Leu Asp Leu Gly Lys His  
 1330 1335 1340

Gly Ala Lys Val Phe Pro Val Leu Ile Gly Asp Thr Thr Val Asn Asp  
 1345 1350 1355 1360

Thr Val Gln Glu Arg Leu Thr Phe Tyr Val Asp Ser Asn Asn Pro Glu

-continued

1365					1370					1375					
Leu	Thr	Leu	Asn	Gln	Glu	Lys	Asp	Gln	Ser	Gly	Tyr	Val	Pro	Val	Tyr
			1380					1385					1390		
Thr	Asn	Lys	Glu	Glu	Phe	Lys	Leu	Gln	Gly	Thr	Ile	Ser	Asp	Asp	Tyr
		1395					1400						1405		
Pro	Tyr	Tyr	Ser	Leu	Leu	Ile	Asn	Asp	Asn	Asn	Val	Asp	Ala	Asn	Trp
		1410					1415					1420			
Asp	Asp	Val	Asp	Tyr	Asn	Gly	Asn	Lys	Asn	Leu	Lys	Lys	Ser	Phe	Ser
1425						1430					1435				1440
His	Ser	Val	Lys	Leu	Lys	Glu	Gly	Lys	Asn	Thr	Phe	Asn	Val	Val	Val
			1445						1450					1455	
Val	Asp	Asn	Asn	Asp	Asn	Arg	Ser	Glu	Val	Gln	Thr	Leu	Val	Val	Tyr
			1460					1465					1470		
Tyr	Lys	Lys	Ala	Gln	Lys	Leu	Ala	Ser	Pro	Gln	Ile	Thr	Ala	Thr	Thr
			1475					1480					1485		
Ala	Ser	Asp	Lys	Lys	Ser	Val	Thr	Val	Thr	Gly	Lys	Ala	Lys	Asp	Gly
			1490				1495					1500			
Asn	Val	Leu	Tyr	Ser	Thr	Asp	Asn	Gly	Asn	Lys	Tyr	Asn	Val	Leu	Pro
1505						1510					1515				1520
Glu	Asp	Gly	Val	Thr	Val	Lys	Asn	Asn	Gly	Lys	Leu	Leu	Phe	Lys	Thr
			1525						1530					1535	
Val	Asp	Lys	Tyr	Gly	Asn	Glu	Ser	Glu	Val	Val	Glu	Tyr	Asp	Val	Lys
			1540					1545					1550		
Thr	Ile	Gly	Lys	Glu	Glu	Ser	Thr	Val	Asp	Lys	Ser	Val	Ala	Gln	Ala
		1555						1560					1565		
Arg	Lys	Asp	Leu	Arg	Lys	Lys	Leu	Asp	Gln	Ala	Arg	Ala	Leu	Gly	Asn
		1570					1575					1580			
Thr	Gly	Lys	Tyr	Thr	His	Glu	Ser	Ala	Lys	Lys	Leu	Ala	Gln	Ala	Arg
1585						1590					1595				1600
Gln	Glu	Ala	Ser	Lys	Ala	Leu	Lys	Asp	Lys	Asn	Ala	Thr	Leu	Gln	Glu
			1605					1610						1615	
Leu	Lys	Gln	Ala	Ser	Glu	Gln	Leu	Glu	Glu	Ala	Ile	Lys	Asn	Leu	Val
			1620					1625					1630		
Glu	Lys	Pro	Val	Asp	Gln	Asn	Lys	Asp	Lys	Asp	Lys	Val	Glu	Asp	Lys
			1635				1640					1645			
Asp	Ser	Gln	Val	Asn	Ala	Leu	Lys	Glu	Lys	Leu	Glu	Glu	Thr	Val	Lys
			1650				1655					1660			
Ala	Gly	Glu	Lys	Phe	Asp	Lys	Asp	Lys	Tyr	Thr	Asp	Asp	Ser	Val	Glu
1665						1670					1675				1680
Lys	Val	Thr	Lys	Ala	Leu	Asp	Glu	Ala	Lys	Val	Val	Leu	Ala	Asn	Lys
			1685					1690					1695		
Asp	Ala	Asn	Ser	Thr	Asp	Val	Gln	Asp	Ala	Ile	Asp	Ser	Ile	Val	Asn
			1700					1705					1710		
Ala	Thr	Lys	Ser	Leu	Lys	Glu	Lys	Gln	Val	Ser	Pro	Glu	Lys	Thr	Thr
			1715					1720					1725		
Gln	Gln	Glu	Asp	Thr	Pro	Lys	Glu	Asn	Lys	Asp	Thr	Glu	Glu	Val	Leu
			1730				1735					1740			
Ala	Ala	Lys	Asn	Ala	Leu	Lys	Glu	Lys	Ala	Asp	Lys	Leu	Ser	His	Leu
1745						1750					1755				1760
Asp	Thr	Thr	Lys	Tyr	Thr	Ser	Glu	Ser	Ala	Glu	Asn	Leu	Ser	Asn	Ala
			1765						1770					1775	
Leu	Lys	Lys	Val	Asn	Gln	Val	Leu	Thr	Asn	Lys	Asp	Ala	Asn	Lys	Ala
			1780					1785					1790		

-continued

Gln Val Gln Glu Ala Leu Asp Ser Leu Ser Gln Ala Glu Lys Asp Leu  
 1795 1800 1805  
 Val Glu Lys Thr Glu Ser Asn Lys Asp Val Glu Thr Ala Lys Glu Gln  
 1810 1815 1820  
 Leu Arg Glu Glu Leu Asn Lys His Lys Asp Glu Asp Lys Ser Gln Tyr  
 1825 1830 1835 1840  
 Thr Asp Asp Ser Ala Lys Val Lys Asp Asn Ala Glu Lys Ile Ser Glu  
 1845 1850 1855  
 Gly Val Leu Asp Ser Lys Asp Ala Gln Ala Asp Glu Val Asn Lys Ala  
 1860 1865 1870  
 Lys Asp Ser Leu Val Glu Ala Glu Lys Gly Leu Val Lys Lys Glu Glu  
 1875 1880 1885  
 Asn Lys Pro Ala Glu Ser Asp Thr Gln Glu Val Asp Lys Ala Arg Glu  
 1890 1895 1900  
 Ala Leu Glu Gln Glu Val Asn Lys Asn Ala Asn Val Asn Leu Asp Gly  
 1905 1910 1915 1920  
 Tyr Thr Pro Glu Ser Gln Asp Lys Phe Lys Glu Ile Leu Asn Gly Val  
 1925 1930 1935  
 Arg Asp Val Leu Asn Asp Lys Asn Ala Ser Ala Ser Ser Leu Glu Lys  
 1940 1945 1950  
 Ala Glu Lys Val Leu Glu Thr Ala Thr Gly Val Leu Thr Gln Val Glu  
 1955 1960 1965  
 His Gln Val Glu Leu Pro Lys Val Glu Gln Pro Val Val Thr Pro Glu  
 1970 1975 1980  
 Lys Lys Gln Thr Glu Gln Glu Glu Ala Lys Lys Ser Glu Ser Ser Ser  
 1985 1990 1995 2000  
 Val Ser Thr Ser Lys Asp Glu Val Lys Glu Pro Glu Glu Lys Lys Gln  
 2005 2010 2015  
 Asp Ala His Ser Val Ser Asp Lys Gly Thr Gly Thr Ser Val Glu Lys  
 2020 2025 2030  
 Lys Gly Gln Thr Pro Ala Asp Ala Leu Ser Gln Val Glu His Gln Ala  
 2035 2040 2045  
 Glu Leu Ser Lys Asn Glu Gln Glu Glu Ala Lys Lys Ser Glu Ser His  
 2050 2055 2060  
 Ser Ala Ser Thr Ser Lys Asp Glu Val Lys Glu Pro Glu Glu Lys Lys  
 2065 2070 2075 2080  
 Gln Asp Ala Glu Ser Val Ser Asp Lys Glu Ser Ser Thr Leu Val Gly  
 2085 2090 2095  
 Lys Lys His Gln Val Ala Arg Ser Ala Gln Glu Ser Ser Lys Lys Asn  
 2100 2105 2110  
 Ala Asp Asn Lys Val Pro Thr His Lys Asn Ser Asn Lys Ala Gln Asn  
 2115 2120 2125  
 Thr Thr Asn Ser Ser Thr Arg Ser Thr Lys Ser Ser Asn Asn Lys Glu  
 2130 2135 2140  
 Leu Pro Lys Thr Gly Glu Arg Glu Thr Phe Phe Gly Leu Leu Val Thr  
 2145 2150 2155 2160  
 Gly Ile Thr Ala Leu Phe Ala Ser Leu Gly Thr Val Leu Arg Ile Lys  
 2165 2170 2175  
 Asn Lys Lys

&lt;210&gt; SEQ ID NO 25

&lt;211&gt; LENGTH: 1774

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Lactobacillus sp.

-continued

&lt;400&gt; SEQUENCE: 25

Met Ala Glu Leu Ala Ala Ala Leu Leu Leu Ser Ala Ser Pro Leu Ala  
 1 5 10 15  
 Gly Thr Phe Gln Ser Ala Ala Phe Val Gln Ala Ala Ser Gln Glu Thr  
 20 25 30  
 Val Ser Pro Arg Ser Ala Ser Arg Ala Ala Leu Thr Lys Tyr Leu Gln  
 35 40 45  
 Gln Glu Gln Arg Tyr Asn Ala Lys Lys Ser Tyr Ser Lys Phe Gln Glu  
 50 55 60  
 Ala Ala Lys Glu Gln Arg Gln Ala Ser Gly Gln Ala Val Ser Lys Lys  
 65 70 75 80  
 Asn Glu Ser Ser Val Arg Val Ile Val Ser Leu Asn Lys Ser Ala Ala  
 85 90 95  
 Phe Asp His Thr Ser Lys Pro Thr Gly Ser Ala Ala Ser Val Lys Lys  
 100 105 110  
 Ile Glu Gln Ala Ser Asp Gln Val Lys Asp Gly Gln Glu Lys Val Ile  
 115 120 125  
 Lys Gln Val Glu Glu Ile Thr Gly Asn Lys Val Arg Arg Gln Phe Gly  
 130 135 140  
 Tyr Leu Val Asn Ala Phe Ser Ile Asp Met Asp Leu Asp Asp Ile Asp  
 145 150 155 160  
 Lys Val Lys Asp Leu Pro Gln Val Lys Asn Val Thr Pro Val Lys Val  
 165 170 175  
 Tyr His Pro Thr Asp Glu Ser Ala Asp Gln Met Ala Gln Val Gln Asp  
 180 185 190  
 Val Trp Gln Glu Gln Lys Leu Lys Gly Glu Gly Met Val Ile Ser Ile  
 195 200 205  
 Ile Asp Thr Gly Ile Asp Ser Ser His Gln Asp Leu Lys Leu Asp Ser  
 210 215 220  
 Gly Val Ser Gly Tyr Asn Tyr Ala Asp Lys Asn Asp Gln Ile Val Asp  
 225 230 235 240  
 Asn Gly Cys Gly Glu Met His Gly Gln His Val Ala Gly Ile Ala Gly  
 245 250 255  
 Ala Asn Gly Gln Val Lys Gly Val Ala Pro Asp Ala Gln Leu Leu Ala  
 260 265 270  
 Met Lys Val Phe Ser Asn Asn Ala Lys Asn Ser Gly Ala Tyr Asp Asp  
 275 280 285  
 Asp Ile Ile Ser Ala Ile Glu Asp Ser Val Lys Leu Gly Ala Asp Val  
 290 295 300  
 Ile Asn Met Ser Leu Gly Ser Val Ser Ser Asp Val Asp Pro Ser Asp  
 305 310 315 320  
 Pro Gln Gln Gln Ala Val Ala Lys Ala Ser Glu Ala Gly Val Ile Asn  
 325 330 335  
 Val Ile Ser Ala Gly Asn Ser Gly Val Ala Gly Ser Thr Ala Asp Gly  
 340 345 350  
 Asn Pro Val Asn Asn Thr Gly Thr Ser Glu Leu Ser Thr Val Gly Thr  
 355 360 365  
 Pro Gly Val Thr Pro Asp Ala Leu Thr Val Ala Ser Ala Glu Asn Ser  
 370 375 380  
 Lys Val Thr Thr Asp Thr Val Lys Asp Glu Leu Gly Gly Val Thr Phe  
 385 390 395 400  
 Ser Ser Asn Ser Glu Leu Lys Gly Ala Ala Gln Val Thr Thr Gln Leu  
 405 410 415

-continued

---

Glu	Ser	Asn	Tyr	Ser	Val	Leu	Thr	Lys	Lys	Leu	Lys	Leu	Val	Asp	Met
			420					425					430		
Gly	Leu	Gly	Gly	Ala	Asp	Asp	Tyr	Thr	Ala	Glu	Lys	Lys	Ala	Glu	Val
		435					440					445			
Lys	Gly	Gln	Leu	Ala	Val	Val	Glu	Arg	Gly	Ser	Tyr	Thr	Phe	Ser	Ala
	450					455					460				
Lys	Val	Ala	Asn	Ala	Lys	Ala	Ala	Gly	Ala	Ala	Gly	Ile	Val	Ile	Tyr
465					470					475					480
Asn	Ser	Glu	Asp	Asp	Gly	Leu	Leu	Ser	Met	Ser	Leu	Asp	Asp	Lys	Thr
				485					490					495	
Phe	Pro	Thr	Leu	Gly	Met	Ser	Lys	Ala	Asp	Gly	Glu	Val	Leu	Ala	Lys
			500					505					510		
Ala	Ala	Lys	Glu	Gly	Lys	Ser	Ile	Lys	Leu	Lys	Phe	Gly	Thr	Ala	Leu
		515					520					525			
Ile	Asp	Asn	Ser	Ser	Ala	Gly	Lys	Met	Ser	Asp	Phe	Thr	Ser	Trp	Gly
	530					535					540				
Pro	Thr	Pro	Asp	Leu	Asp	Phe	Lys	Pro	Glu	Ile	Thr	Ala	Pro	Gly	Gly
545					550					555					560
Lys	Ile	Tyr	Ser	Leu	Ala	Asn	Asp	Asn	Lys	Tyr	Gln	Gln	Met	Ser	Gly
				565					570					575	
Thr	Ser	Met	Ala	Ser	Pro	Phe	Val	Ala	Gly	Ser	Glu	Ala	Leu	Ile	Leu
			580					585					590		
Gln	Gly	Ile	Lys	Lys	Gln	Gly	Leu	Asn	Leu	Ser	Gly	Glu	Glu	Leu	Val
		595					600					605			
Gln	Phe	Ala	Lys	Asn	Ser	Ala	Met	Asn	Thr	Ser	His	Pro	Val	Tyr	Asp
	610					615					620				
Thr	Glu	His	Thr	Lys	Glu	Ile	Ile	Ser	Pro	Arg	Arg	Gln	Gly	Ser	Gly
625					630					635					640
Glu	Ile	Asn	Val	Lys	Asp	Ala	Ile	Asn	Asn	Thr	Val	Glu	Val	Lys	Ala
				645					650					655	
Ala	Asn	Gly	Asn	Gly	Ala	Ala	Ala	Leu	Lys	Glu	Ile	Gly	Arg	Gln	Thr
			660					665					670		
Thr	Phe	Lys	Val	Thr	Leu	Thr	Asn	His	Gly	Lys	Lys	Ala	Gln	Thr	Tyr
		675					680					685			
Ala	Val	Asp	Asn	Tyr	Gly	Gly	Pro	Tyr	Thr	Gln	Ala	Thr	Glu	Ala	Lys
	690					695					700				
Ser	Gly	Glu	Ile	Tyr	Asp	Thr	Lys	Ile	Val	Lys	Gly	Gln	Leu	Thr	Thr
705					710					715					720
Glu	Thr	Pro	Lys	Val	Thr	Val	Gln	Pro	Gly	Glu	Ser	Val	Asp	Val	Ser
				725					730					735	
Phe	Thr	Leu	Thr	Leu	Pro	Tyr	Ser	Phe	Gln	Arg	Gln	Asn	Phe	Val	Glu
			740					745					750		
Gly	Tyr	Val	Gly	Phe	Glu	Ala	Glu	Asp	Gln	Ala	Thr	Pro	Asn	Leu	Val
		755					760					765			
Leu	Pro	Tyr	Met	Gly	Phe	Phe	Gly	Ser	Tyr	Ser	Gln	Ala	Ser	Val	Ser
	770					775					780				
Ala	Pro	Met	Leu	Tyr	Glu	Gly	Gly	Asn	Ser	Asn	Leu	Ile	Asn	Thr	Ile
					790					795					800
His	Ser	Leu	Val	Gly	Val	Met	Phe	Ser	Asn	Asn	Asn	Asp	Ile	Leu	Gly
				805					810				815		
His	Thr	Gly	Tyr	Glu	Gly	Asp	Asp	Tyr	Ser	Lys	Tyr	Thr	Asp	Pro	Asp
			820					825					830		
Leu	Ile	Ala	Ile	Ser	Pro	Asn	Gly	Asp	Gly	Ser	Arg	Asp	Tyr	Ala	Tyr
			835				840					845			

-continued

---

Pro Val Leu Phe Phe Asp Arg Asn Tyr Lys Glu Tyr Thr Glu Thr Ile  
 850 855 860

Thr Asp Ala Gln Gly Asn Lys Val Lys Ser Leu Gly Val Gly Lys Glu  
 865 870 875 880

Gly Thr Lys Asp Tyr Tyr Ser Ser Ser Ser Gly Glu Trp Thr Thr His  
 885 890 895

Ser Leu Asp Lys Trp Asp Gly Thr Asp Ala Asp Gly Gln Val Val Lys  
 900 905 910

Asp Gly Gln Tyr Ile Tyr Lys Val Glu Phe Thr Pro Ala Ile Gly Gly  
 915 920 925

Ser Lys Gln Glu Leu Asn Ile Pro Val Lys Val Asp Thr Gln Ala Pro  
 930 935 940

Glu Val Ser Asp Leu Gln Val Thr Lys Asp Gly Lys Leu Arg Leu Lys  
 945 950 955 960

Ala Lys Asp Ser Gly Ser Gly Leu Asp Met Thr Met Phe Val Ala Ala  
 965 970 975

Val Asn Gly Glu Glu Gln Lys Leu Ala Leu Ala Pro Val Lys Gly Glu  
 980 985 990

Ser Asn Val Tyr Glu Ser Thr Ser Ala Leu Thr Gly Leu Lys Asp Gly  
 995 1000 1005

Lys Asn Gln Val Glu Thr Val Leu Ala Asp Tyr Ala Gly Asn Val Gly  
 1010 1015 1020

Tyr Ala Ala Thr Phe Ser Ser Gln Asn Asn Asp Ala Asp Asn Lys Leu  
 1025 1030 1035 1040

Leu Leu Phe Asn Leu Ala Asp Gly Gln Lys Ile Thr Ser Gln Ser Pro  
 1045 1050 1055

Ala Tyr Asp Gln Glu Lys Glu Thr Tyr Thr Val Thr Gly Thr Tyr Lys  
 1060 1065 1070

Lys Asn Ala Lys Leu Lys Phe Asn Asp Val Glu Ala Glu Ser Asp Lys  
 1075 1080 1085

Asn Gly Tyr Phe Glu Val Lys Leu Pro Val Lys Asp Gly Gln Asn Gln  
 1090 1095 1100

Leu Leu Ile Lys Asp Gly Asp Gln Ile Leu Glu Ala Val Asn Phe Thr  
 1105 1110 1115 1120

Val Lys Ala Glu Gly Pro Lys Val Ser Val Asp Glu Glu Arg Ser Gly  
 1125 1130 1135

Arg Ile Leu Ala Lys Asp Asp Ser Tyr Thr Leu Ser Gly Thr Val Ser  
 1140 1145 1150

Gly Leu Gly Glu Ser Gly Lys Leu Glu Leu Thr Asn Leu Ser Asp Lys  
 1155 1160 1165

Ser Lys Thr Asn Lys Leu Thr Val Asp Gln Asp Gly Lys Phe Ser Gln  
 1170 1175 1180

Lys Val Asp Leu Asn Tyr Gly Asp Asn Pro Phe Glu Leu Thr Ala Thr  
 1185 1190 1195 1200

Asp Ala Asp Gly Asn Val Thr Lys Lys Asp Val Thr Ile Phe Thr Ala  
 1205 1210 1215

Arg Ser Tyr Thr Tyr Asn Lys Asp Met Leu Thr Phe Asp Asn Ile Ala  
 1220 1225 1230

Ser Asp Leu Thr Val Ile Gly Lys Thr Thr Pro Asp Tyr Asp Glu Lys  
 1235 1240 1245

Asp His Ser Phe Thr Val Thr Gly Lys Leu Ala Tyr Pro Val Ala Arg  
 1250 1255 1260

Phe Gln Leu Asn Gly Asp Asp Val Lys Tyr Asp Pro Asp Thr Leu Lys

-continued

1265	1270	1275	1280
Phe Ser Tyr Thr Ile Lys Asp Leu Lys Asn Gly Asn His Ser Leu Thr	1285	1290	1295
Ala Leu Val Gln Asp Pro Arg Leu Asn Asp Gly Lys Pro Val Val Glu	1300	1305	1310
Trp Gly Tyr Lys Leu Trp Val Asp Leu Ala Ala Pro Ser Leu Gln Leu	1315	1320	1325
Glu Gly Met Ser Leu Gly Glu Asp Gly Gln Leu Ala Val Tyr Thr Asn	1330	1335	1340
Lys Asp Val Tyr Asp Leu Lys Ala Thr Ile Asn Asp Asn Leu Ser Gly	1345	1350	1355
Tyr Ser Leu Gln Val Gly Ser Asp Thr Ala Tyr Gln Asp Lys Thr Tyr	1365	1370	1375
Lys Val Phe Asn Glu Asp Phe Phe Lys Asn Arg Asp Ala Val Lys Val	1380	1385	1390
Ser Tyr Pro Ile Lys Ala Glu Lys Asp Gly Phe Arg Lys Val Lys Val	1395	1400	1405
Thr Leu Thr Asp Gly Ser Asp Asn Lys Thr Glu Gln Asp Phe Ile Leu	1410	1415	1420
Tyr Asn His Gln Ala Asp Leu Glu Ala Pro Glu Val Ser Ala Ser Glu	1425	1430	1435
Ser Lys Lys Thr Asn Gln Ala Val Gln Leu Lys Val Gly Asn Leu Ser	1445	1450	1455
Asp Val Gln Lys Ser Ala Gly Lys Phe Lys Ala Ala Asp Leu Tyr Tyr	1460	1465	1470
Ser Val Asp Gly Lys Thr Trp Thr Lys Leu Asp Lys Asp Thr Val Gln	1475	1480	1485
Val Ala Glu Asn Gly Lys Val Glu Phe Lys Tyr Gln Asp Val Tyr Gly	1490	1495	1500
Asn Glu Ser Lys Val Thr Thr Tyr Glu Val Lys Asn Ile Val Lys Glu	1505	1510	1515
Val Ala Ala Gln Pro Glu Leu Lys Leu Thr Pro Asp Gly Glu Gly Lys	1525	1530	1535
Val Lys Ala Val Leu Ala Phe Asp Lys Lys Asp Val Asp Lys Asp Phe	1540	1545	1550
Asn His Ile Lys Tyr Ser Leu Asp Gly Gly Lys Ser Trp Thr Asp Tyr	1555	1560	1565
Lys Asp Ala Phe Thr Leu Thr His Asn Gly Thr Val Glu Phe Lys Ser	1570	1575	1580
Tyr Asp Asp Ala Gly Asn Glu Gly Gln Val Tyr Thr Ser Val Val Lys	1585	1590	1595
Val Glu Arg Lys Leu Pro Ala Pro Asp Leu Thr Gly Thr Val Glu Ala	1605	1610	1615
Asp Lys Ser Val Glu Val Lys Ala Gly Asn Ser Ser Ala Lys Lys Thr	1620	1625	1630
Ser Ala Lys Lys Asn Lys Lys Ala Ser Lys Lys Ala Ser Lys Lys Thr	1635	1640	1645
Val Lys Lys Thr Lys Thr Tyr Lys Lys Val Lys Leu Thr Lys Leu Thr	1650	1655	1660
Lys Val Tyr Asn Lys Lys Gly Lys Val Val Gly Lys Leu Lys Lys Lys	1665	1670	1675
Thr Ser Ile Lys Leu Leu Ser Lys Lys Gln Lys Leu His Gly Lys Tyr	1685	1690	1695



-continued

Tyr Tyr Arg Val Gly Lys Asn Arg Tyr Ile Leu Ala Ser Asn Leu Pro  
                   1700                                  1705                                  1710  
 Lys Lys Thr Lys Lys Val Lys Gln Val Arg Ala Arg Lys Asn Ala Lys  
                   1715                                  1720                                  1725  
 Val Tyr Asn Lys Lys Gly Lys Val Val Gly His Leu Lys Lys Lys Gln  
                   1730                                  1735                                  1740  
 Lys Val Lys Leu Leu Ser Lys Lys Gln Lys Leu His Gly Lys Tyr Tyr  
                   1745                                  1750                                  1755                                  1760  
 Tyr Arg Ile Gly Lys Asn Arg Tyr Val Asn Ala Asn Val Leu  
                                   1765                                  1770

<210> SEQ ID NO 26  
 <211> LENGTH: 485  
 <212> TYPE: PRT  
 <213> ORGANISM: Lactobacillus acidophilus

<400> SEQUENCE: 26

Met Val Glu Asn Lys Trp Leu His Ala Arg Lys Met Glu Val Arg Met  
   1                  5                                  10                                  15  
 Leu Ile Ile Glu Ala Ile Tyr Val Phe Ser Met Phe Leu Ser Leu Val  
                   20                                  25                                  30  
 Phe Tyr Phe Pro Leu Phe Val Ile Glu Phe Lys Ile Ala Ile Ala Phe  
                   35                                  40                                  45  
 Thr Phe Leu Val Met Ile Gly Glu Leu Phe Glu Ile Lys Phe Lys Asn  
                   50                                  55                                  60  
 Glu Glu Ser Lys Asp Arg Ile Asp Ile Lys Glu His Gly Leu Met Lys  
                   65                                  70                                  75                                  80  
 Pro Cys Phe Phe His Lys Glu Glu Lys Arg Val Lys Ala Lys Ser Trp  
                                   85                                  90                                  95  
 Asn Trp Asn Met Ile Leu Asn Ile Gln Leu Ile Ile Asn Ile Leu Ile  
                                   100                                  105                                  110  
 Ala Gly Tyr Leu Leu Val Arg Glu Asn Lys Asn Leu Asp Ile Gln Ile  
                   115                                  120                                  125  
 Ile Phe Gly Ile Ile Leu Leu Tyr Ile Ile Ile Ala Arg Leu Phe Ile  
                   130                                  135                                  140  
 Lys Asn Gln Tyr Ile Glu Lys Phe Asn Leu Val Leu Glu Ile Ile Cys  
                   145                                  150                                  155                                  160  
 Leu Pro Ile Leu Leu Thr Tyr Tyr Leu Asn Trp Leu Val Ile Ser Leu  
                                   165                                  170                                  175  
 Val His Phe Leu Pro Ala Ile Lys Leu Glu Ile Ile Thr Ile Tyr Leu  
                   180                                  185                                  190  
 Val Val Ile Leu Leu Tyr Leu Leu Pro Thr Ser Val Val Ala Phe Gly  
                   195                                  200                                  205  
 Lys Ile His Asn Gly Tyr Leu Arg Ile Ala Ala Ser Ile Tyr Leu Phe  
                   210                                  215                                  220  
 Leu Val Phe Leu Ser Ser Ile Asn Ser Ser Leu Ser Val Asn Val Asp  
                   225                                  230                                  235                                  240  
 Phe Ile Asp Asn Leu Leu Lys Val Asn Val Val Ser Gly Met Ala Phe  
                                   245                                  250                                  255  
 Leu Ile Leu Thr Pro Phe Leu Leu Arg Gln Trp Gly Phe Lys Phe Arg  
                   260                                  265                                  270  
 Met Asn Val Phe Pro Arg Lys Gln Glu Asn Phe Gln Leu Leu Val Leu  
                   275                                  280                                  285  
 Ile Leu Leu Val Leu Phe Ala Ala Trp Leu Thr Phe Phe Asn Thr Tyr  
                   290                                  295                                  300

-continued

Val Tyr Ile Ala Thr Val Pro Glu Gln Leu Phe Phe Asn Trp Asp Leu  
 305 310 315 320  
 Ser Ile Leu Ala Pro Thr Gln Trp Thr Val Leu Arg Ser Ala Gly Ala  
 325 330 335  
 Ala Ile Phe Glu Glu Thr Glu Arg Tyr Leu Ile Leu Ile Leu Leu Leu  
 340 345 350  
 Tyr Ile Ala Arg Asn Ser Arg Phe Gln Ile Gln Ile Ala Ile Phe Phe  
 355 360 365  
 Ser Ala Val Gln Phe Gly Leu Leu His Met Thr His Phe Leu Asp Ala  
 370 375 380  
 Asp Ala Asn Val Ser Ser Ile Phe Tyr Glu Val Leu Tyr Thr Phe Gly  
 385 390 395 400  
 Tyr Gly Cys Phe Leu Ala Val Leu Tyr Leu Tyr Ser Gly Gln Ile Trp  
 405 410 415  
 Leu Ser Met Leu Ser His Phe Thr Leu Asp Leu Val Ser Tyr Ser Val  
 420 425 430  
 Gly Asn Gly Gly Val Gly Phe Leu Ser Leu Tyr Gly Asn Val Glu Gly  
 435 440 445  
 Ile Gly Ala Ala Leu Val Leu Ala Val Asn Leu Leu Val Val Phe Leu  
 450 455 460  
 Met Leu Trp Gly Lys Arg Lys Ile Val Met Gln Asn Asn Ala Arg Ile  
 465 470 475 480  
 Leu Ile Glu Arg Ile  
 485

&lt;210&gt; SEQ ID NO 27

&lt;211&gt; LENGTH: 407

&lt;212&gt; TYPE: PRT

<213> ORGANISM: *Lactococcus lactis*

&lt;400&gt; SEQUENCE: 27

Met Ala Lys Ala Asn Ile Gly Lys Leu Leu Leu Thr Gly Val Val Gly  
 1 5 10 15  
 Gly Ala Ile Ala Leu Gly Gly Ser Ala Ile Tyr Gln Ser Thr Thr Asn  
 20 25 30  
 Gln Leu Gly Asn Ala Asn Arg Ser Asn Thr Thr Ser Thr Lys Val Ser  
 35 40 45  
 Asn Val Ser Val Asn Val Asn Thr Asp Val Thr Ser Ala Ile Lys Lys  
 50 55 60  
 Val Ser Asn Ser Val Val Ser Val Met Asn Tyr Gln Lys Gln Asn Ser  
 65 70 75 80  
 Gln Ser Asp Phe Ser Ser Ile Phe Gly Gly Asn Ser Gly Ser Ser Ser  
 85 90 95  
 Ala Asn Asp Gly Leu Gln Leu Ser Ser Glu Gly Ser Gly Val Ile Tyr  
 100 105 110  
 Lys Lys Ser Gly Gly Asp Ala Tyr Val Val Thr Asn Tyr His Val Ile  
 115 120 125  
 Ala Gly Asn Ser Ser Leu Asp Val Leu Leu Ser Gly Gly Gln Lys Val  
 130 135 140  
 Lys Ala Thr Val Val Gly Tyr Asp Glu Tyr Thr Asp Leu Ala Val Leu  
 145 150 155 160  
 Lys Ile Ser Ser Asp His Val Lys Asp Val Ala Thr Phe Ala Asp Ser  
 165 170 175  
 Ser Lys Leu Thr Ile Gly Glu Pro Ala Ile Ala Val Gly Ser Pro Leu  
 180 185 190

-continued

Gly Ser Gln Phe Ala Asn Thr Ala Thr Glu Gly Ile Leu Ser Ala Thr  
 195 200 205  
 Ser Arg Gln Val Thr Leu Thr Gln Glu Asn Gly Gln Thr Thr Ser Ile  
 210 215 220  
 Asn Ala Ile Gln Thr Asp Ala Ala Ile Asn Pro Gly Asn Ser Gly Gly  
 225 230 235 240  
 Ala Leu Ile Asn Ile Glu Gly Gln Val Ile Gly Ile Thr Gln Ser Lys  
 245 250 255  
 Ile Thr Thr Thr Glu Asp Gly Ser Thr Ser Val Glu Gly Leu Gly Phe  
 260 265 270  
 Ala Ile Pro Ser Asn Asp Val Val Asn Ile Ile Asn Lys Leu Glu Thr  
 275 280 285  
 Asp Gly Lys Ile Ser Arg Pro Ala Leu Gly Ile Arg Met Val Asp Leu  
 290 295 300  
 Ser Gln Leu Ser Thr Asn Asp Ser Ser Gln Leu Lys Leu Pro Ser Ser  
 305 310 315 320  
 Val Thr Gly Gly Val Val Val Tyr Ser Val Gln Ala Gly Leu Pro Ala  
 325 330 335  
 Ala Thr Ala Gly Leu Lys Ala Gly Asp Val Ile Thr Lys Val Gly Asp  
 340 345 350  
 Thr Ala Val Thr Ser Ser Thr Asp Leu Gln Ser Ala Leu Tyr Ser His  
 355 360 365  
 Asn Ile Asn Asp Thr Val Lys Val Thr Tyr Tyr Arg Asp Gly Lys Ser  
 370 375 380  
 Ala Thr Ala Asn Val Lys Leu Ser Lys Ser Thr Ser Asp Leu Glu Thr  
 385 390 395 400  
 Asn Ser Pro Ser Ser Ser Asn  
 405

&lt;210&gt; SEQ ID NO 28

&lt;211&gt; LENGTH: 409

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Lactococcus lactis

&lt;400&gt; SEQUENCE: 28

Met Ala Lys Ala Asn Ile Gly Lys Leu Leu Thr Gly Val Val Gly  
 1 5 10 15  
 Gly Ala Ile Ala Leu Gly Gly Ser Ala Ile Tyr Gln Ser Thr Thr Asn  
 20 25 30  
 Gln Ser Ala Asn Asn Ser Arg Ser Asn Thr Thr Ser Thr Lys Val Ser  
 35 40 45  
 Asn Val Ser Val Asn Val Asn Thr Asp Val Thr Ser Ala Ile Lys Lys  
 50 55 60  
 Val Ser Asn Ser Val Val Ser Val Met Asn Tyr Gln Lys Asp Asn Ser  
 65 70 75 80  
 Gln Ser Ser Asp Phe Ser Ser Ile Phe Gly Gly Asn Ser Gly Ser Ser  
 85 90 95  
 Ser Ser Thr Asp Gly Leu Gln Leu Ser Ser Glu Gly Ser Gly Val Ile  
 100 105 110  
 Tyr Lys Lys Ser Gly Gly Asp Ala Tyr Val Val Thr Asn Tyr His Val  
 115 120 125  
 Ile Ala Gly Asn Ser Ser Leu Asp Val Leu Leu Ser Gly Gly Gln Lys  
 130 135 140  
 Val Lys Ala Ser Val Val Gly Tyr Asp Glu Tyr Thr Asp Leu Ala Val  
 145 150 155 160

-continued

---

```

Leu Lys Ile Ser Ser Glu His Val Lys Asp Val Ala Thr Phe Ala Asp
          165                               170                   175

Ser Ser Lys Leu Thr Ile Gly Glu Pro Ala Ile Ala Val Gly Ser Pro
          180                               185                   190

Leu Gly Ser Gln Phe Ala Asn Thr Ala Thr Glu Gly Ile Leu Ser Ala
          195                               200                   205

Thr Ser Arg Gln Val Thr Leu Thr Gln Glu Asn Gly Gln Thr Thr Asn
          210                               215                   220

Ile Asn Ala Ile Gln Thr Asp Ala Ala Ile Asn Pro Gly Asn Ser Gly
          225                               230                   235                   240

Gly Ala Leu Ile Asn Ile Glu Gly Gln Val Ile Gly Ile Thr Gln Ser
          245                               250                   255

Lys Ile Thr Thr Thr Glu Asp Gly Ser Thr Ser Val Glu Gly Leu Gly
          260                               265                   270

Phe Ala Ile Pro Ser Asn Asp Val Val Asn Ile Ile Asn Lys Leu Glu
          275                               280                   285

Ala Asp Gly Lys Ile Ser Arg Pro Ala Leu Gly Ile Arg Met Val Asp
          290                               295                   300

Leu Ser Gln Leu Ser Thr Asn Asp Ser Ser Gln Leu Lys Leu Pro Ser
          305                               310                   315                   320

Ser Val Thr Gly Gly Val Val Val Tyr Ser Val Gln Ser Gly Leu Pro
          325                               330                   335

Ala Ala Ser Ala Gly Leu Lys Ala Gly Asp Val Ile Thr Lys Val Gly
          340                               345                   350

Asp Thr Ala Val Thr Ser Ser Thr Asp Leu Gln Ser Ala Leu Tyr Ser
          355                               360                   365

His Asn Ile Asn Asp Thr Val Lys Val Thr Tyr Tyr Arg Asp Gly Lys
          370                               375                   380

Ser Asn Thr Ala Asp Val Lys Leu Ser Lys Ser Thr Ser Asp Leu Glu
          385                               390                   395                   400

Thr Ser Ser Pro Ser Ser Ser Asn Tyr
          405

```

```

<210> SEQ ID NO 29
<211> LENGTH: 402
<212> TYPE: PRT
<213> ORGANISM: Streptococcus mutans

```

```

<400> SEQUENCE: 29

```

```

Met Asn Asn Thr Lys Ser His Pro Phe Leu Lys Trp Phe Ile Pro Phe
  1           5           10           15

Leu Val Ile Phe Leu Thr Phe Ile Leu Gly Val Ile Ser Thr Leu Thr
          20           25           30

Phe Asn Trp Ile Thr Gly Asn Lys Ser Phe Ser Asn Asn Gly Lys Thr
          35           40           45

Thr Val Ser Asn Val Ile Tyr Asp Thr Lys Ser Asn Thr Thr Lys Ala
          50           55           60

Val Lys Asn Val Lys Asn Thr Val Val Ser Val Ile Asn Tyr Gln Lys
          65           70           75           80

Thr Asp Asn Ser Tyr Tyr Asn Tyr Asp Ser Gly Ser Gln Glu Lys Asn
          85           90           95

Lys Ser Glu Asp Gly Leu Gly Val Tyr Gly Glu Gly Ser Gly Val Ile
          100          105          110

Tyr Lys Lys Asp Gly Asp Ser Ala Tyr Leu Val Thr Asn Asn His Val
          115          120          125

```

-continued

Val Lys Asp Ala Glu Lys Leu Glu Ile Met Met Ala Asn Gly Lys Lys  
 130 135 140  
 Val Val Gly Lys Leu Val Gly Ser Asp Thr Tyr Ser Asp Leu Ala Val  
 145 150 155 160  
 Ile Lys Ile Ser Ser Lys Tyr Val Thr Thr Val Ala Glu Phe Ala Asn  
 165 170 175  
 Ser Asp Lys Ile Lys Val Gly Glu Pro Ala Ile Ala Ile Gly Ser Pro  
 180 185 190  
 Leu Gly Ser Asp Tyr Ala Asn Ser Val Thr Glu Gly Ile Val Ser Ser  
 195 200 205  
 Leu Ser Arg Thr Val Thr Ser Gln Asn Glu Asn Gly Glu Thr Ile Ser  
 210 215 220  
 Thr Asn Ala Ile Gln Thr Asp Ala Ala Ile Asn Pro Gly Asn Ser Gly  
 225 230 235 240  
 Gly Ala Leu Ile Asn Ile Lys Gly Gln Val Ile Gly Ile Asn Ser Ser  
 245 250 255  
 Lys Ile Ala Ser Ser Asn Asn Ser Asn Ser Gly Val Ala Val Glu Gly  
 260 265 270  
 Met Gly Phe Ala Ile Pro Ser Asn Asp Val Val Ser Ile Ile Asn Gln  
 275 280 285  
 Leu Glu Glu Asn Gly Glu Val Val Arg Pro Ala Leu Gly Ile Ser Met  
 290 295 300  
 Ala Asn Leu Ser Glu Ala Ser Thr Ser Gly Arg Asp Thr Leu Lys Ile  
 305 310 315 320  
 Pro Ser Asp Val Thr Ser Gly Ile Val Val Leu Ser Thr Gln Ser Gly  
 325 330 335  
 Met Pro Ala Asp Gly Lys Leu Lys Lys Tyr Asp Val Ile Thr Glu Ile  
 340 345 350  
 Asp Gly Lys Lys Val Ala Ser Ile Ser Asp Leu Gln Ser Ile Leu Tyr  
 355 360 365  
 Lys His Lys Lys Gly Asp Lys Ile Lys Leu Thr Phe Tyr Arg Glu Lys  
 370 375 380  
 Asp Lys Gln Thr Val Glu Ile Gln Leu Thr Lys Thr Ser Gln Asp Leu  
 385 390 395 400

Asn His

&lt;210&gt; SEQ ID NO 30

&lt;211&gt; LENGTH: 413

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Lactobacillus helveticus

&lt;400&gt; SEQUENCE: 30

Met Val Glu Asn Gln Asn Asn Asn Gln Asn Gln Pro Arg Lys Lys Ser  
 1 5 10 15  
 Gly Asn Lys Ile Ile Ala Thr Ala Ala Ile Phe Gly Val Val Gly Gly  
 20 25 30  
 Leu Val Gly Gly Gly Val Ser Tyr Tyr Ala Met Asp Gln Met Asn Asn  
 35 40 45  
 Gly Gln Gly Asn Gly Ala Ala Gln Ile Ser Ile Ser Ser Ser Ser  
 50 55 60  
 Lys Val Ser Glu Lys Ser Ala Lys Asn Gly Gly Thr Met Thr Ala Ala  
 65 70 75 80  
 Tyr Asn Asp Val Lys Gly Ala Val Val Ser Val Ile Asn Leu Lys Arg  
 85 90 95  
 Gln Ser Ala Ser Ser Gly Thr Asp Ser Leu Tyr Asn Ser Leu Phe Gly

-continued

100					105					110						
Asp	Asp	Ser	Asp	Ser	Ser	Ser	Ser	Ser	Lys	Asn	Gly	Lys	Leu	Glu	Thr	Tyr
		115						120						125		
Ser	Glu	Gly	Ser	Gly	Val	Val	Tyr	Met	Lys	Ser	Asn	Gly	Lys	Gly	Tyr	
	130						135					140				
Ile	Val	Thr	Asn	Asn	His	Val	Ile	Ser	Gly	Ser	Asp	Ala	Val	Gln	Val	
145						150					155				160	
Leu	Leu	Ala	Asn	Gly	Lys	Thr	Val	Asn	Ala	Lys	Val	Val	Gly	Lys	Asp	
				165					170					175		
Ser	Thr	Thr	Asp	Leu	Ala	Val	Leu	Ser	Ile	Asp	Ala	Lys	Tyr	Val	Thr	
			180					185					190			
Gln	Thr	Ala	Gln	Phe	Gly	Asp	Ser	Lys	His	Leu	Glu	Ala	Gly	Gln	Thr	
		195					200					205				
Val	Ile	Ala	Val	Gly	Ser	Pro	Leu	Gly	Ser	Glu	Tyr	Ala	Ser	Thr	Val	
	210						215				220					
Thr	Gln	Gly	Ile	Ile	Ser	Ala	Pro	Ala	Arg	Thr	Ile	Ser	Thr	Ser	Ser	
225						230					235				240	
Gly	Asn	Gln	Gln	Thr	Val	Ile	Gln	Thr	Asp	Ala	Ala	Ile	Asn	Pro	Gly	
				245					250					255		
Asn	Ser	Gly	Gly	Ala	Leu	Val	Asn	Ser	Ala	Gly	Gln	Val	Ile	Gly	Ile	
				260					265					270		
Asn	Ser	Met	Lys	Leu	Ala	Gln	Ser	Ser	Asp	Gly	Thr	Ser	Val	Glu	Gly	
		275					280						285			
Met	Ala	Phe	Ala	Ile	Pro	Ser	Asn	Glu	Val	Val	Thr	Ile	Val	Asn	Glu	
	290						295					300				
Leu	Val	Lys	Lys	Gly	Lys	Ile	Thr	Arg	Pro	Gln	Leu	Gly	Val	Arg	Val	
305						310					315				320	
Ile	Ala	Leu	Gln	Gly	Ile	Pro	Glu	Gly	Tyr	Arg	Ser	Arg	Leu	Lys	Ile	
				325					330					335		
Lys	Ser	Asn	Leu	Lys	Asn	Gly	Ile	Tyr	Ile	Ala	Phe	Val	Ser	Arg	Asn	
			340					345					350			
Gly	Ser	Ala	Ala	Asn	Ala	Gly	Ile	Lys	Ser	Gly	Asp	Val	Ile	Thr	Lys	
			355				360					365				
Val	Asp	Gly	Lys	Lys	Val	Glu	Asp	Val	Ala	Ser	Leu	His	Ser	Ile	Leu	
	370						375					380				
Tyr	Ser	His	Lys	Val	Gly	Asp	Thr	Val	Asn	Val	Thr	Val	Asn	Arg	Asn	
385						390					395				400	
Gly	Lys	Asp	Val	Asp	Met	Lys	Val	Lys	Leu	Glu	Gly	Asn				
				405					410							

&lt;210&gt; SEQ ID NO 31

&lt;211&gt; LENGTH: 423

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Lactobacillus acidophilus

&lt;400&gt; SEQUENCE: 31

Met	Ile	Leu	Gly	Asn	Met	Arg	Gly	Glu	Leu	Ser	Met	Val	Glu	Asn	Gln
1				5					10					15	
Asn	Asn	Asn	Gln	Arg	Pro	Arg	Lys	Asn	Ser	Asn	Ala	Lys	Ile	Ile	Thr
			20					25					30		
Thr	Ala	Ala	Ile	Val	Gly	Val	Val	Gly	Gly	Leu	Ile	Gly	Gly	Gly	Val
			35				40					45			
Ser	Tyr	Tyr	Ala	Ala	Asp	Gln	Met	Asn	Asn	Ala	Thr	Asp	Thr	Thr	Thr
	50					55					60				
Ala	Gln	Thr	Ser	Val	Ser	Ser	Asn	Ser	Ser	Lys	Val	Ser	Glu	Lys	Ser

-continued

65	70	75	80
Ala Lys Thr Ser Gly Thr Met Thr Thr Ala Tyr Asn Asp Val Lys Gly	85	90	95
Ala Val Val Ser Val Ile Asn Leu Lys Arg Gln Ser Ser Ser Ser Ser	100	105	110
Ala Asn Ser Leu Tyr Ser Ser Leu Phe Gly Asp Asp Ser Asp Ser Ser	115	120	125
Ser Gly Lys Ser Gly Lys Leu Glu Thr Tyr Ser Glu Gly Ser Ser Val	130	135	140
Val Tyr Met Lys Ser Asn Gly Lys Gly Tyr Ile Val Thr Asn Asn His	145	150	155
Val Ile Ser Gly Ser Asp Ala Val Gln Val Gln Leu Ala Asn Gly Lys	165	170	175
Thr Val Ser Ala Lys Val Val Gly Lys Asp Ser Thr Thr Asp Leu Ala	180	185	190
Val Leu Ser Ile Asp Ala Lys Tyr Val Thr Gln Thr Ala Glu Phe Gly	195	200	205
Asp Ser Lys Ser Leu Gln Ala Gly Gln Thr Val Ile Ala Val Gly Ser	210	215	220
Pro Leu Gly Ser Glu Tyr Ala Ser Thr Val Thr Gln Gly Ile Ile Ser	225	230	235
Ala Pro Ala Arg Thr Ile Ser Thr Ser Ser Gly Asn Gln Gln Thr Val	245	250	255
Ile Gln Thr Asp Ala Ala Ile Asn Pro Gly Asn Ser Gly Gly Ala Leu	260	265	270
Val Asn Ser Ala Gly Gln Val Ile Gly Ile Asn Ser Met Lys Leu Ala	275	280	285
Gln Ser Ser Asp Gly Thr Ser Val Glu Gly Met Gly Phe Ala Ile Pro	290	295	300
Ser Asn Glu Val Val Thr Ile Val Asn Glu Leu Val Lys Lys Gly Lys	305	310	315
Ile Thr Arg Pro Gln Leu Gly Val Arg Val Val Ala Leu Glu Gly Ile	325	330	335
Pro Glu Ala Tyr Arg Ser Arg Leu Lys Ile Lys Ser Asn Leu Lys Ser	340	345	350
Gly Ile Tyr Val Ala Ser Ile Asn Lys Asn Ser Ser Ala Ala Asn Ala	355	360	365
Gly Met Lys Ser Gly Asp Val Ile Thr Lys Val Asp Gly Lys Lys Val	370	375	380
Asp Asp Val Ala Ser Leu His Ser Ile Leu Tyr Ser His Lys Val Gly	385	390	395
Asp Thr Val Asn Ile Thr Ile Asn Arg Asn Gly Arg Asp Val Asn Leu	405	410	415
Lys Val Lys Leu Glu Gly Asn	420		

&lt;210&gt; SEQ ID NO 32

&lt;211&gt; LENGTH: 420

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Lactobacillus plantarum

&lt;400&gt; SEQUENCE: 32

Met Ala Asn Lys Ser Leu Ile Lys Val Ala Val Thr Ala Leu Val Ala	1	5	10	15
---	---	---	----	----

Gly Leu Ile Gly Gly Gly Val Ala Tyr Gly Gly Ile Asn Tyr Phe Gln

-continued

20					25					30					
Asn	Asn	Asn	Ile	Ala	Thr	Ser	Ser	Thr	Ser	Val	Pro	Thr	Gly	Ser	Asn
		35					40					45			
Lys	Ser	Gly	Ser	Thr	Ser	Thr	Thr	Asn	Val	Lys	Val	Asn	Val	Ser	Ser
	50					55					60				
Gln	Ala	Thr	Lys	Val	Phe	Glu	Asn	Asn	Lys	Ala	Ala	Val	Val	Ser	Val
	65					70					75				80
Ile	Asn	Leu	Gln	Lys	Lys	Ser	Ser	Ser	Ser	Ser	Trp	Ser	Gly	Ile	Leu
				85							90			95	
Gly	Gly	Asp	Asp	Ser	Ser	Gly	Ser	Asp	Ser	Ser	Ser	Ser	Ser	Asp	Ser
			100					105						110	
Ser	Ser	Ser	Lys	Leu	Glu	Glu	Tyr	Ser	Glu	Gly	Ser	Gly	Leu	Ile	Tyr
			115				120					125			
Lys	Lys	Ser	Gly	Asp	Ala	Ala	Tyr	Ile	Val	Thr	Asn	Asn	His	Val	Val
	130					135					140				
Ser	Gly	Ser	Ser	Ala	Ile	Arg	Val	Ile	Met	Ser	Asp	Gly	Thr	Lys	Leu
	145					150					155				160
Ser	Ala	Lys	Ile	Val	Gly	Thr	Asp	Ser	Val	Thr	Asp	Leu	Ala	Val	Leu
				165					170					175	
Lys	Ile	Asn	Ser	Ser	Lys	Val	Thr	Lys	Thr	Ala	Ser	Phe	Gly	Asn	Ser
			180					185					190		
Asp	Asn	Ile	Lys	Val	Gly	Glu	Thr	Ala	Leu	Ala	Ile	Gly	Ser	Pro	Met
		195					200					205			
Gly	Ser	Asn	Tyr	Ala	Thr	Thr	Leu	Thr	Gln	Gly	Ile	Ile	Ser	Ala	Lys
		210				215					220				
Lys	Arg	Thr	Val	Ala	Thr	Thr	Asn	Thr	Ser	Gly	Gln	Thr	Thr	Gly	Tyr
				230							235				240
Ala	Thr	Val	Ile	Gln	Thr	Asp	Thr	Ala	Ile	Asn	Ser	Gly	Asn	Ser	Gly
				245					250					255	
Gly	Pro	Leu	Phe	Asn	Ile	Ala	Gly	Gln	Val	Ile	Gly	Ile	Asn	Ser	Met
			260					265					270		
Lys	Leu	Ala	Ser	Asp	Asn	Ser	Gly	Thr	Ser	Val	Glu	Gly	Met	Gly	Phe
		275					280					285			
Ala	Ile	Pro	Ser	Asn	Glu	Val	Val	Lys	Ile	Ile	Asn	Glu	Leu	Val	Gln
		290				295					300				
Lys	Gly	Glu	Val	Val	Arg	Pro	Ala	Leu	Gly	Val	Ala	Thr	Tyr	Asp	Leu
				310							315				320
Ser	Asn	Ile	Ser	Ser	Ser	Asp	Gln	Lys	Ser	Val	Leu	Lys	Leu	Pro	Thr
				325					330					335	
Ser	Val	Thr	Lys	Gly	Val	Val	Ile	Met	Lys	Thr	Tyr	Ser	Gly	Ser	Pro
			340					345					350		
Ala	Lys	Ala	Ala	Gly	Leu	Thr	Lys	Tyr	Asp	Val	Ile	Thr	Glu	Leu	Gly
		355					360					365			
Gly	Lys	Lys	Val	Thr	Ser	Leu	Ala	Thr	Leu	Arg	Ser	Ala	Leu	Tyr	Ala
				370			375				380				
His	Ser	Val	Asn	Asp	Thr	Val	Thr	Val	Lys	Tyr	Tyr	His	Asn	Gly	Lys
				385		390					395				400
Leu	Lys	Thr	Ala	Asn	Met	Lys	Leu	Thr	Glu	Thr	Thr	Lys	Thr	Leu	Thr
				405					410					415	
Lys	Gln	Ser	Asn												
			420												

&lt;210&gt; SEQ ID NO 33

&lt;211&gt; LENGTH: 411



-continued

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Streptococcus thermophilus

&lt;400&gt; SEQUENCE: 33

Met Glu Lys Phe Asn Trp Lys Lys Ile Val Ala Pro Ile Ala Met Leu  
 1 5 10 15  
 Ile Ile Gly Leu Leu Gly Gly Leu Leu Gly Ala Phe Ile Leu Leu Thr  
 20 25 30  
 Ala Ala Gly Val Ser Phe Thr Asn Thr Thr Asp Thr Gly Val Lys Thr  
 35 40 45  
 Ala Lys Thr Val Tyr Thr Asn Ile Thr Asp Thr Thr Lys Ala Val Lys  
 50 55 60  
 Lys Val Gln Asn Ala Val Val Ser Val Ile Asn Tyr Gln Glu Gly Ser  
 65 70 75 80  
 Ser Ser Asp Ser Leu Asn Asp Leu Tyr Gly Arg Ile Phe Gly Gly Gly  
 85 90 95  
 Asp Ser Ser Asp Ser Ser Gln Glu Asn Ser Lys Asp Ser Asp Gly Leu  
 100 105 110  
 Gln Val Ala Gly Glu Gly Ser Gly Val Ile Tyr Lys Lys Asp Gly Lys  
 115 120 125  
 Glu Ala Tyr Ile Val Thr Asn Asn His Val Val Asp Gly Ala Lys Lys  
 130 135 140  
 Leu Glu Ile Met Leu Ser Asp Gly Ser Lys Ile Thr Gly Glu Leu Val  
 145 150 155 160  
 Gly Lys Asp Thr Tyr Ser Asp Leu Ala Val Val Lys Val Ser Ser Asp  
 165 170 175  
 Lys Ile Thr Thr Val Ala Glu Phe Ala Asp Ser Asn Ser Leu Thr Val  
 180 185 190  
 Gly Glu Lys Ser Ile Ala Ile Gly Ser Pro Leu Gly Thr Glu Tyr Ala  
 195 200 205  
 Asn Ser Val Thr Glu Gly Ile Val Ser Ser Leu Ser Arg Thr Ile Thr  
 210 215 220  
 Met Gln Asn Asp Asn Gly Glu Thr Val Ser Thr Ile Ala Ile Gln Thr  
 225 230 235 240  
 Asp Ala Ala Ile Asn Pro Gly Asn Ser Gly Gly Ala Leu Val Asn Ile  
 245 250 255  
 Glu Gly Gln Val Ile Gly Ile Asn Ser Ser Lys Ile Ser Ser Thr Ser  
 260 265 270  
 Ala Val Ala Gly Ser Ala Val Glu Gly Met Gly Phe Ala Ile Pro Ser  
 275 280 285  
 Asn Asp Val Val Glu Ile Ile Asn Gln Leu Glu Lys Asp Gly Lys Val  
 290 295 300  
 Thr Arg Pro Ala Leu Gly Ile Ser Ile Ala Asp Leu Asn Ser Leu Ser  
 305 310 315 320  
 Ser Ser Ala Thr Ser Lys Leu Asp Leu Pro Asp Glu Val Lys Ser Gly  
 325 330 335  
 Val Val Val Gly Ser Val Gln Lys Gly Met Pro Ala Asp Gly Lys Leu  
 340 345 350  
 Gln Glu Tyr Asp Val Ile Thr Glu Ile Asp Gly Lys Lys Ile Gly Ser  
 355 360 365  
 Lys Thr Asp Ile Gln Thr Asn Leu Tyr Ser His Ser Ile Gly Asp Thr  
 370 375 380  
 Ile Lys Val Thr Phe Tyr Arg Gly Lys Asp Lys Lys Thr Val Asp Leu  
 385 390 395 400

-continued

Lys Leu Thr Lys Ser Thr Glu Asp Ile Ser Asp  
 405 410

<210> SEQ ID NO 34  
 <211> LENGTH: 411  
 <212> TYPE: PRT  
 <213> ORGANISM: Streptococcus thermophilus

<400> SEQUENCE: 34

Met Lys Lys Phe Asn Trp Lys Lys Ile Val Ala Pro Ile Ala Met Leu  
 1 5 10 15  
 Ile Ile Gly Leu Leu Gly Gly Leu Leu Gly Ala Phe Ile Leu Leu Thr  
 20 25 30  
 Ala Ala Gly Val Ser Phe Thr Asn Thr Thr Asp Thr Gly Val Lys Thr  
 35 40 45  
 Ala Lys Thr Val Tyr Thr Asn Ile Thr Asp Thr Thr Lys Ala Val Lys  
 50 55 60  
 Lys Val Gln Asn Ala Val Val Ser Val Ile Asn Tyr Gln Glu Gly Ser  
 65 70 75 80  
 Ser Ser Asp Ser Leu Asn Asp Leu Tyr Gly Arg Ile Phe Gly Gly Gly  
 85 90 95  
 Asp Ser Ser Asp Ser Ser Gln Glu Asn Ser Lys Asp Ser Asp Gly Leu  
 100 105 110  
 Gln Val Ala Gly Glu Gly Ser Gly Val Ile Tyr Lys Lys Asp Gly Lys  
 115 120 125  
 Glu Ala Tyr Ile Val Thr Asn Asn His Val Val Asp Gly Ala Lys Lys  
 130 135 140  
 Leu Glu Ile Met Leu Ser Asp Gly Ser Lys Ile Thr Gly Glu Leu Val  
 145 150 155 160  
 Gly Lys Asp Thr Tyr Ser Asp Leu Ala Val Val Lys Val Ser Ser Asp  
 165 170 175  
 Lys Ile Thr Thr Val Ala Glu Phe Ala Asp Ser Asn Ser Leu Thr Val  
 180 185 190  
 Gly Glu Lys Ala Ile Ala Ile Gly Ser Pro Leu Gly Thr Glu Tyr Ala  
 195 200 205  
 Asn Ser Val Thr Glu Gly Ile Val Ser Ser Leu Ser Arg Thr Ile Thr  
 210 215 220  
 Met Gln Asn Asp Asn Gly Glu Thr Val Ser Thr Asn Ala Ile Gln Thr  
 225 230 235 240  
 Asp Ala Ala Ile Asn Pro Gly Asn Ser Gly Gly Ala Leu Val Asn Ile  
 245 250 255  
 Glu Gly Gln Val Ile Gly Ile Asn Ser Ser Lys Ile Ser Ser Thr Ser  
 260 265 270  
 Ala Val Ala Gly Ser Ala Val Glu Gly Met Gly Phe Ala Ile Pro Ser  
 275 280 285  
 Asn Asp Val Val Glu Ile Ile Asn Gln Leu Glu Lys Asp Gly Lys Val  
 290 295 300  
 Thr Arg Pro Ala Leu Gly Ile Ser Ile Ala Asp Leu Asn Ser Leu Ser  
 305 310 315 320  
 Ser Ser Ala Thr Ser Lys Leu Asp Leu Pro Asp Glu Val Lys Ser Gly  
 325 330 335  
 Val Val Val Gly Ser Val Gln Lys Gly Met Pro Ala Asp Gly Lys Leu  
 340 345 350  
 Gln Glu Tyr Asp Val Ile Thr Glu Ile Asp Gly Lys Lys Ile Ser Ser  
 355 360 365

-continued

---

Lys Thr Asp Ile Gln Thr Asn Leu Tyr Ser His Ser Ile Gly Asp Thr  
 370 375 380

Ile Lys Val Thr Phe Tyr Arg Gly Lys Asp Lys Lys Thr Val Asp Leu  
 385 390 395 400

Lys Leu Thr Lys Ser Thr Glu Asp Ile Ser Asp  
 405 410

<210> SEQ ID NO 35  
 <211> LENGTH: 407  
 <212> TYPE: PRT  
 <213> ORGANISM: *Lactococcus lactis*

<400> SEQUENCE: 35

Met Ala Lys Ala Asn Ile Gly Lys Leu Leu Leu Thr Gly Val Val Gly  
 1 5 10 15

Gly Ala Ile Ala Leu Gly Gly Ser Ala Ile Tyr Gln Ser Thr Thr Asn  
 20 25 30

Gln Leu Gly Asn Ala Asn Arg Ser Asn Thr Thr Ser Thr Lys Val Ser  
 35 40 45

Asn Val Ser Val Asn Val Asn Thr Asp Val Thr Ser Ala Ile Lys Lys  
 50 55 60

Val Ser Asn Ser Val Val Ser Val Met Asn Tyr Gln Lys Gln Asn Ser  
 65 70 75 80

Gln Ser Asp Phe Ser Ser Ile Phe Gly Gly Asn Ser Gly Ser Ser Ser  
 85 90 95

Ala Asn Asp Gly Leu Gln Leu Ser Ser Glu Gly Ser Gly Val Ile Tyr  
 100 105 110

Lys Lys Ser Gly Gly Asp Ala Tyr Val Val Thr Asn Tyr His Val Ile  
 115 120 125

Ala Gly Asn Ser Ser Leu Asp Val Leu Leu Ser Gly Gly Gln Lys Val  
 130 135 140

Lys Ala Thr Val Val Gly Tyr Asp Glu Tyr Thr Asp Leu Ala Val Leu  
 145 150 155 160

Lys Ile Ser Ser Asp His Val Lys Asp Val Ala Thr Phe Ala Asp Ser  
 165 170 175

Ser Lys Leu Thr Ile Gly Glu Pro Ala Ile Ala Val Gly Ser Pro Leu  
 180 185 190

Gly Ser Gln Phe Ala Asn Thr Ala Thr Glu Gly Ile Leu Ser Ala Thr  
 195 200 205

Ser Arg Gln Val Thr Leu Thr Gln Glu Asn Gly Gln Thr Thr Ser Ile  
 210 215 220

Asn Ala Ile Gln Thr Asp Ala Ala Ile Asn Pro Gly Asn Ser Gly Gly  
 225 230 235 240

Ala Leu Ile Asn Ile Glu Gly Gln Val Ile Gly Ile Thr Gln Ser Lys  
 245 250 255

Ile Thr Thr Thr Glu Asp Gly Ser Thr Ser Val Glu Gly Leu Gly Phe  
 260 265 270

Ala Ile Pro Ser Asn Asp Val Val Asn Ile Ile Asn Lys Leu Glu Thr  
 275 280 285

Asp Gly Lys Ile Ser Arg Pro Ala Leu Gly Ile Arg Met Val Asp Leu  
 290 295 300

Ser Gln Leu Ser Thr Asn Asp Ser Ser Gln Leu Lys Leu Pro Ser Ser  
 305 310 315 320

Val Thr Gly Gly Val Val Val Tyr Ser Val Gln Ala Gly Leu Pro Ala  
 325 330 335

-continued

Ala Thr Ala Gly Leu Lys Ala Gly Asp Val Ile Thr Lys Val Gly Asp  
 340 345 350

Thr Ala Val Thr Ser Ser Thr Asp Leu Gln Ser Ala Leu Tyr Ser His  
 355 360 365

Asn Ile Asn Asp Thr Val Lys Val Thr Tyr Tyr Arg Asp Gly Lys Ser  
 370 375 380

Ala Thr Ala Asn Val Lys Leu Ser Lys Ser Thr Ser Asp Leu Glu Thr  
 385 390 395 400

Asn Ser Pro Ser Ser Ser Asn  
 405

&lt;210&gt; SEQ ID NO 36

&lt;211&gt; LENGTH: 361

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Actinobacillus actinomycetemcomitans

&lt;400&gt; SEQUENCE: 36

Asn Cys Cys Val Lys Gly Asn Ser Ile Tyr Pro Gln Lys Thr Ser Thr  
 1 5 10 15

Lys Gln Thr Gly Leu Met Leu Asp Ile Ala Arg His Phe Tyr Ser Pro  
 20 25 30

Glu Val Ile Lys Ser Phe Ile Asp Thr Ile Ser Leu Ser Gly Gly Asn  
 35 40 45

Phe Leu His Leu His Phe Ser Asp His Glu Asn Tyr Ala Ile Glu Ser  
 50 55 60

His Leu Leu Asn Gln Arg Ala Glu Asn Ala Val Gln Gly Lys Asp Gly  
 65 70 75 80

Ile Tyr Ile Asn Pro Tyr Thr Gly Lys Pro Phe Leu Ser Tyr Arg Gln  
 85 90 95

Leu Asp Asp Ile Lys Ala Tyr Ala Lys Ala Lys Gly Ile Glu Leu Ile  
 100 105 110

Pro Glu Leu Asp Ser Pro Asn His Met Thr Ala Ile Phe Lys Leu Val  
 115 120 125

Gln Lys Asp Arg Gly Val Lys Tyr Leu Gln Gly Leu Lys Ser Arg Gln  
 130 135 140

Val Asp Asp Glu Ile Asp Ile Thr Asn Ala Asp Ser Ile Thr Phe Met  
 145 150 155 160

Gln Ser Leu Met Ser Glu Val Ile Asp Ile Phe Gly Asp Thr Ser Gln  
 165 170 175

His Phe His Ile Gly Gly Asp Glu Phe Gly Tyr Ser Val Glu Ser Asn  
 180 185 190

His Glu Phe Ile Thr Tyr Ala Asn Lys Leu Ser Tyr Phe Leu Glu Lys  
 195 200 205

Lys Gly Leu Lys Thr Arg Met Trp Asn Asp Gly Leu Ile Lys Asn Thr  
 210 215 220

Phe Glu Gln Ile Asn Pro Asn Ile Glu Ile Thr Tyr Trp Ser Tyr Asp  
 225 230 235 240

Gly Asp Thr Gln Asp Lys Asn Glu Ala Ala Glu Arg Arg Asp Met Arg  
 245 250 255

Val Ser Leu Pro Glu Leu Leu Ala Lys Gly Phe Thr Val Leu Asn Tyr  
 260 265 270

Asn Ser Tyr Tyr Leu Tyr Ile Val Pro Lys Ala Ser Pro Thr Phe Ser  
 275 280 285

Gln Asp Ala Ala Phe Ala Ala Lys Asp Val Ile Lys Asn Trp Asp Leu  
 290 295 300

-continued

Gly Val Trp Asp Gly Arg Asn Thr Lys Asn Arg Val Gln Asn Thr His  
 305 310 315 320  
 Glu Ile Ala Gly Ala Ala Leu Ser Ile Trp Gly Glu Asp Ala Lys Ala  
 325 330 335  
 Leu Lys Asp Glu Thr Ile Gln Lys Asn Thr Lys Ser Leu Leu Glu Ala  
 340 345 350  
 Val Ile His Lys Thr Asn Gly Asp Glu  
 355 360

<210> SEQ ID NO 37  
 <211> LENGTH: 377  
 <212> TYPE: PRT  
 <213> ORGANISM: Actinobacillus pleuropneumoniae  
 <400> SEQUENCE: 37

Met Lys Lys Ala Ile Thr Leu Phe Thr Leu Leu Cys Ala Val Leu Leu  
 1 5 10 15  
 Ser Phe Ser Thr Ala Thr Tyr Ala Asn Ala Met Asp Leu Pro Lys Lys  
 20 25 30  
 Glu Ser Gly Leu Thr Leu Asp Ile Ala Arg Arg Phe Tyr Thr Val Asp  
 35 40 45  
 Thr Ile Lys Gln Phe Ile Asp Thr Ile His Gln Ala Gly Gly Thr Phe  
 50 55 60  
 Leu His Leu His Phe Ser Asp His Glu Asn Tyr Ala Leu Glu Ser Ser  
 65 70 75 80  
 Tyr Leu Glu Gln Arg Glu Glu Asn Ala Thr Glu Lys Asn Gly Thr Tyr  
 85 90 95  
 Phe Asn Pro Lys Thr Asn Lys Pro Phe Leu Thr Tyr Lys Gln Leu Asn  
 100 105 110  
 Glu Ile Ile Tyr Tyr Ala Lys Glu Arg Asn Ile Glu Ile Val Pro Glu  
 115 120 125  
 Val Asp Ser Pro Asn His Met Thr Ala Ile Phe Asp Leu Leu Thr Leu  
 130 135 140  
 Lys His Gly Lys Glu Tyr Val Lys Gly Leu Lys Ser Pro Tyr Ile Ala  
 145 150 155 160  
 Glu Glu Ile Asp Ile Asn Asn Pro Glu Ala Val Glu Val Ile Lys Thr  
 165 170 175  
 Leu Ile Gly Glu Val Ile Tyr Ile Phe Gly His Ser Ser Arg His Phe  
 180 185 190  
 His Ile Gly Gly Asp Glu Phe Ser Tyr Ala Val Glu Asn Asn His Glu  
 195 200 205  
 Phe Ile Arg Tyr Val Asn Thr Leu Asn Asp Phe Ile Asn Ser Lys Gly  
 210 215 220  
 Leu Ile Thr Arg Val Trp Asn Asp Gly Leu Ile Lys Asn Asn Leu Ser  
 225 230 235 240  
 Glu Leu Asn Lys Asn Ile Glu Ile Thr Tyr Trp Ser Tyr Asp Gly Asp  
 245 250 255  
 Ala Gln Ala Lys Glu Asp Ile Gln Tyr Arg Arg Glu Ile Arg Ala Asp  
 260 265 270  
 Leu Pro Glu Leu Leu Ala Asn Gly Phe Lys Val Leu Asn Tyr Asn Ser  
 275 280 285  
 Tyr Tyr Leu Tyr Phe Val Pro Lys Ser Gly Ser Asn Ile His Asn Asp  
 290 295 300  
 Gly Lys Tyr Ala Ala Glu Asp Val Leu Asn Asn Trp Thr Leu Gly Lys  
 305 310 315 320

-continued

Trp Asp Gly Lys Asn Ser Ser Asn His Val Gln Asn Thr Gln Asn Ile  
 325 330 335

Ile Gly Ser Ser Leu Ser Ile Trp Gly Glu Arg Ser Ser Ala Leu Asn  
 340 345 350

Glu Gln Thr Ile Gln Gln Ala Ser Lys Asn Leu Leu Lys Ala Val Ile  
 355 360 365

Gln Lys Thr Asn Asp Pro Lys Ser His  
 370 375

&lt;210&gt; SEQ ID NO 38

&lt;211&gt; LENGTH: 325

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Lactococcus lactis

&lt;400&gt; SEQUENCE: 38

Met Glu Lys Gly Leu Leu Val Asp Ile Gly Arg Lys Tyr Trp Ser Ile  
 1 5 10 15

Ala Glu Leu Lys Arg Leu Val Leu Leu Leu Gln Glu His Lys Leu Thr  
 20 25 30

His Leu Gln Leu His Leu Asn Glu Asn Glu Gly Phe Ala Leu Asn Phe  
 35 40 45

Thr Asp Ser Pro Val Ser Lys Lys Tyr Ser Glu Asn Met Leu Lys Glu  
 50 55 60

Leu Lys Glu Phe Ala Lys Thr His Glu Ile Thr Leu Ile Pro Asp Phe  
 65 70 75 80

Asp Ser Pro Gly His Met Gly Ser Leu Leu Glu Gln Asn Pro Glu Phe  
 85 90 95

Ala Leu Pro Asp Ser Asn Gln Gln Ala Val Asp Val Thr Asn Pro Ala  
 100 105 110

Val Ile Asp Trp Ile Met Gly Ile Ile Asp Lys Ile Val Asp Ile Phe  
 115 120 125

Pro Asp Ser Asp Thr Phe His Ile Gly Ala Asp Glu Phe Ile Asp Phe  
 130 135 140

Arg Gln Ile Glu Lys Tyr Pro Tyr Leu Val Glu Lys Thr Arg Glu Lys  
 145 150 155 160

Tyr Gly Asn Lys Ala Ser Gly Leu Glu Phe Tyr Tyr Asp Tyr Val Asn  
 165 170 175

Gln Leu Thr Glu His Leu Gln Lys Lys Gly Lys Gln Val Arg Ile Trp  
 180 185 190

Asn Asp Gly Phe Leu Arg Lys Asp Leu Gln Ser Leu Val Pro Leu Asn  
 195 200 205

Lys Asn Val Glu Val Cys Tyr Trp Thr Asn Trp Asp Lys Gly Met Ala  
 210 215 220

Glu Val Lys Glu Trp Leu Thr Lys Gly Tyr Thr Leu Ile Asn Phe Cys  
 225 230 235 240

Asp Asn Asp Leu Tyr Tyr Val Leu Gly Glu Glu Ala Gly Tyr Ser Tyr  
 245 250 255

Pro Thr Ala Glu Lys Leu Glu Arg Glu Gly Lys Ile Gln Lys Phe Ser  
 260 265 270

Gly Gln Gln Tyr Leu Asn Gln Glu Glu Met Lys Ala Val Arg Gly Thr  
 275 280 285

Tyr Phe Ser Ile Trp Ala Asp Asn Ala Ala Ala Lys Ser Val Ser Glu  
 290 295 300

Ile Leu Asp Asp Leu Ser Lys Val Leu Pro Val Phe Met Lys Ile Tyr  
 305 310 315 320

-continued

Gly Gly Asn Asp Glu  
325

<210> SEQ ID NO 39  
<211> LENGTH: 526  
<212> TYPE: PRT  
<213> ORGANISM: Lactobacillus casei

<400> SEQUENCE: 39

Met Val Leu Ser Leu Ser Gln Pro Pro Lys Gln Val Ala Ala Ala Asp  
1 5 10 15

Asn Thr Leu Lys Ser Val Phe Ser Ile Asp Ala Gly Arg Lys Phe Phe  
20 25 30

Ser Ala Asp Gln Leu Lys Met Ile Ile Asp Arg Ala His Thr Asp Gly  
35 40 45

Tyr Thr Asp Val Gln Val Leu Leu Gly Asn Asp Ala Leu Arg Leu Leu  
50 55 60

Leu Asp Asp Met Ser Val Thr Ile Asn Gly Lys Thr Tyr Gly Ser Asp  
65 70 75 80

Val Val Lys Gln Ala Ile Gln Ala Gly Asn Lys Ala Tyr Tyr Asp Asp  
85 90 95

Pro Asn Gly Asn Ala Leu Thr Gln Thr Asp Met Asp Ala Val Leu Lys  
100 105 110

Tyr Ala Ala Ala Arg Asp Ile Asn Ile Ile Pro Val Ile Asn Ser Pro  
115 120 125

Gly His Met Asp Ala Ile Leu Thr Ala Met Ala Gln Leu Gly Ile Lys  
130 135 140

Asn Pro Ala Phe Asn Gly Ser Lys Arg Thr Val Asp Leu Asn Asn Asp  
145 150 155 160

Thr Ala Ile Ala Phe Thr Lys Ala Leu Leu Gln Lys Tyr Val Met Tyr  
165 170 175

Phe Lys Gly His Ala Thr Ile Phe Asn Phe Gly Ser Asp Glu Tyr Ala  
180 185 190

Asn Asp Val Asp Thr Gly Gly Trp Ala Lys Leu Gln Gln Ser Gly Thr  
195 200 205

Tyr Lys Lys Phe Val Ala Tyr Val Asn Asp Leu Ala Ala Met Ala Lys  
210 215 220

Asn Ala Ser Leu Lys Pro Met Val Phe Asn Asp Gly Ile Tyr Tyr Asp  
225 230 235 240

Asn Asn Thr Ser Phe Gly Thr Phe Asp Lys Asp Leu Ile Val Ser Tyr  
245 250 255

Trp Thr Ala Gly Trp Gly Gly Tyr Asp Val Ala Lys Pro Glu Phe Leu  
260 265 270

Thr Asp Lys Gly Leu Lys Ile Met Asn Thr Asn Asp Gly Trp Tyr Trp  
275 280 285

Val Leu Gly Arg Val Asp Gly Asp Leu Tyr Ser Tyr Lys Thr Ala Leu  
290 295 300

Ala Ser Leu Ala Ser Lys Lys Phe Thr Asp Val Pro Gly Ala Ser Ser  
305 310 315 320

Ala Val Pro Ile Ile Gly Ser Val Gln Ala Val Trp Ala Asp Asp Pro  
325 330 335

Ser Ala Gln Leu Asp Met Pro Ala Leu Leu Lys Leu Met Asp Gln Phe  
340 345 350

Ser Thr Ala Tyr Ala Pro Tyr Leu Val Arg Pro Ala Asp Tyr Ser Lys  
355 360 365

-continued

---

Val Asp Ala Ala Ile Ala Ala Val Pro Arg Gln Leu Asn Gln Tyr Thr  
 370 375 380

Glu Ala Ser Val Ala Lys Leu Asp Ala Ala Leu Asn Ala Val Val Arg  
 385 390 395 400

Gly Lys Lys Ala Thr Asp Gln Ala Leu Val Asp Gly Tyr Ala Gln Thr  
 405 410 415

Ile Thr Val Ala Ile Lys Ala Leu Gln Leu Arg Pro Ala Asp Tyr Thr  
 420 425 430

Lys Val Asp Ala Ala Ile Ala Ala Ala Lys Lys Leu Asp Arg Ser His  
 435 440 445

Tyr Gln Asp Leu Ser Ala Val Asp Ala Ala Leu Ala Ala Val Asn Arg  
 450 455 460

Asn Leu Ser Ile Thr Gln Gln Ala Gln Ala Asp Thr Met Ala Ala Lys  
 465 470 475 480

Ile Thr Ala Ala Ile Ala Ala Leu Val Leu Lys Pro Ala Pro Gln Pro  
 485 490 495

Asp Pro Arg Gln Gln Gln Val Pro Thr Lys Thr Ile Val Asn Pro Asp  
 500 505 510

Arg Tyr Leu Pro Lys Thr Ala Glu Ala Ser Arg Val Gly Asn  
 515 520 525

&lt;210&gt; SEQ ID NO 40

&lt;211&gt; LENGTH: 325

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Lactococcus lactis

&lt;400&gt; SEQUENCE: 40

Met Glu Lys Gly Leu Leu Val Asp Ile Gly Arg Lys Tyr Trp Ser Ile  
 1 5 10 15

Ala Glu Leu Lys Arg Leu Val Leu Leu Leu Gln Glu His Lys Leu Thr  
 20 25 30

His Leu Gln Leu His Leu Asn Glu Asn Glu Gly Phe Ala Leu Asn Phe  
 35 40 45

Thr Asp Ser Pro Val Ser Lys Lys Tyr Ser Glu Asn Met Leu Lys Glu  
 50 55 60

Leu Lys Glu Phe Ala Lys Thr His Glu Ile Thr Leu Ile Pro Asp Phe  
 65 70 75 80

Asp Ser Pro Gly His Met Gly Ser Leu Leu Glu Gln Asn Pro Glu Phe  
 85 90 95

Ala Leu Pro Asp Ser Asn Gln Gln Ala Val Asp Val Thr Asn Pro Ala  
 100 105 110

Val Ile Asp Trp Ile Met Gly Ile Ile Asp Lys Ile Val Asp Ile Phe  
 115 120 125

Pro Asp Ser Asp Thr Phe His Ile Gly Ala Asp Glu Phe Ile Asp Phe  
 130 135 140

Arg Gln Ile Glu Lys Tyr Pro Tyr Leu Val Glu Lys Thr Arg Glu Lys  
 145 150 155 160

Tyr Gly Asn Lys Ala Ser Gly Leu Glu Phe Tyr Tyr Asp Tyr Val Asn  
 165 170 175

Gln Leu Thr Glu His Leu Gln Lys Lys Gly Lys Gln Val Arg Ile Trp  
 180 185 190

Asn Asp Gly Phe Leu Arg Lys Asp Leu Gln Ser Leu Val Pro Leu Asn  
 195 200 205

Lys Asn Val Glu Val Cys Tyr Trp Thr Asn Trp Asp Lys Gly Met Ala  
 210 215 220



-continued

Glu Val Lys Glu Trp Leu Thr Lys Gly Tyr Thr Leu Ile Asn Phe Cys  
 225 230 235 240  
 Asp Asn Asp Leu Tyr Tyr Val Leu Gly Glu Glu Ala Gly Tyr Ser Tyr  
 245 250 255  
 Pro Thr Ala Glu Lys Leu Glu Arg Glu Gly Lys Ile Gln Lys Phe Ser  
 260 265 270  
 Gly Gln Gln Tyr Leu Asn Gln Glu Glu Met Lys Ala Val Arg Gly Thr  
 275 280 285  
 Tyr Phe Ser Ile Trp Ala Asp Asn Ala Ala Ala Lys Ser Val Ser Glu  
 290 295 300  
 Ile Leu Asp Asp Leu Ser Lys Val Leu Pro Val Phe Met Lys Ile Tyr  
 305 310 315 320  
 Gly Gly Asn Asp Glu  
 325

<210> SEQ ID NO 41  
 <211> LENGTH: 639  
 <212> TYPE: PRT  
 <213> ORGANISM: Streptomyces sp.

<400> SEQUENCE: 41

Met Asp Met Arg Met Ala Arg Arg Arg Thr Ile Gly Ala Val Val Thr  
 1 5 10 15  
 Ala Leu Ala Ala Ala Leu Leu Pro Trp Gln Ser Ala Thr Ala Glu Gly  
 20 25 30  
 Gly Ser Ala Ala Ala Ala Pro Pro Glu Val Leu Pro Thr Leu Arg Glu  
 35 40 45  
 Trp Gln Gly Gly Gln Gly Glu Phe Thr Leu Thr Asp Arg Ala Gly Ile  
 50 55 60  
 Val Leu Asp Gly Val Arg Asp Ser Arg Thr Ala Ala Asp Ala Arg Arg  
 65 70 75 80  
 Phe Ala Gly Glu Leu Asn Gly Lys Ala Ser Val Ser Gln Gly Arg Ala  
 85 90 95  
 Ala Arg Pro Gly Asp Ile Val Leu Arg Gln Asp Pro Ala Gln Lys Gly  
 100 105 110  
 Leu Leu Gly Ala Glu Gly Tyr Arg Leu Thr Val Gly Thr Arg Ile Thr  
 115 120 125  
 Val Thr Ala Ala Thr Ser Thr Gly Val Phe Tyr Gly Thr Arg Thr Val  
 130 135 140  
 Leu Gln Leu Leu Asn Asp Asp Gly Arg Ala Ala Arg Gly Ser Ala Thr  
 145 150 155 160  
 Asp Val Pro Ala Tyr Arg Glu Arg Gly Val Gly Val Cys Ala Cys Tyr  
 165 170 175  
 Ile Asn Ile Ser Thr Gln Trp Phe Glu Arg Leu Met Lys Asp Met Ala  
 180 185 190  
 Ser Gln Lys Leu Asn Gln Leu Trp Ile Glu Ala Lys Val Lys Ser Asp  
 195 200 205  
 Thr Asp Pro Ala Ser Ala Phe Trp Gly Tyr Tyr Thr Lys Pro Gln Val  
 210 215 220  
 Arg Thr Leu Val Ala Met Ala Arg Lys Tyr His Ile Glu Leu Val Pro  
 225 230 235 240  
 Glu Ile Asn Ser Pro Gly His Met Asp Thr Tyr Leu Glu Asn His Pro  
 245 250 255  
 Glu Leu Gln Leu Lys Asp Arg Asp Gly Val Ala Ser Pro Pro Arg Leu  
 260 265 270

-continued

---

Asp	Ile	Ser	Arg	Pro	Glu	Ala	Leu	Ala	Tyr	Tyr	Thr	Ser	Met	Val	Asp
		275					280					285			
Glu	Ala	Leu	Lys	Val	Trp	Asp	Ser	Arg	Tyr	Trp	His	Met	Gly	Ala	Asp
	290					295					300				
Glu	Tyr	Met	Ile	Gly	Ser	Ser	Tyr	Pro	Asp	Tyr	Pro	Gln	Leu	Gln	Ala
305					310					315					320
Ala	Ala	Arg	Ala	Lys	Phe	Gly	Ala	Ser	Ala	Thr	Pro	Asp	Asp	Leu	Phe
				325					330					335	
Thr	Asp	Phe	Ile	Asn	Gln	Val	Asn	Ala	His	Val	Lys	Ala	Asp	Gly	Arg
			340					345						350	
Ser	Leu	Arg	Ile	Trp	Asn	Asp	Gly	Leu	Ala	Gly	Lys	Asn	Ala	Val	Val
		355					360					365			
Pro	Leu	Asp	Arg	Asp	Ile	Thr	Val	Glu	His	Trp	Leu	Ser	Gly	Gly	Ser
	370					375						380			
Ile	Gln	Gln	Pro	Ser	Ser	Leu	Leu	Ala	Glu	Gly	Arg	Pro	Val	Met	Asn
385						390				395					400
Ser	Ala	Tyr	Ser	Leu	Tyr	Leu	Val	Arg	Gly	Gly	Phe	Thr	Met	Gln	Thr
				405					410					415	
Gln	Lys	Leu	Tyr	Glu	Ser	Asp	Trp	Thr	Pro	Leu	Arg	Phe	Glu	Gly	Gln
			420					425					430		
Thr	Leu	Thr	Gln	Gly	Ala	Ala	Asn	Leu	Thr	Gly	Ala	Lys	Ile	Ser	Leu
		435					440					445			
Trp	Pro	Asp	Ser	Ala	Ala	Ala	Glu	Thr	Glu	Asn	Glu	Val	Glu	Thr	Lys
	450					455					460				
Val	Phe	Met	Pro	Leu	Arg	Phe	Val	Ala	Gln	Ala	Thr	Trp	Gly	Gly	Pro
465					470					475					480
Lys	Pro	Ser	Pro	Thr	Tyr	Ala	Gly	Phe	Glu	Ala	Leu	Ala	Arg	Lys	Ile
				485					490					495	
Gly	His	Ala	Pro	Gly	Trp	Glu	Asn	Thr	Asp	Arg	Thr	Pro	Leu	Ala	Asp
			500					505					510		
Gly	Thr	Tyr	Arg	Leu	Thr	Thr	Gly	Ala	Lys	Ala	Leu	Ala	Pro	Thr	Ala
		515					520					525			
Asp	Ala	Gly	Val	Ser	Leu	Val	Lys	Asn	Ser	Ala	Ala	Ser	Trp	Ala	Leu
	530					535					540				
Thr	Ala	Thr	Ala	Asp	Gly	Tyr	Tyr	Thr	Val	Arg	Ser	Thr	Glu	Ser	Gly
545					550					555					560
Gln	Cys	Leu	Asp	Ala	Val	Arg	Gly	Lys	Lys	Tyr	Leu	Gly	Ala	Pro	Leu
				565					570					575	
Glu	Val	Gly	Ala	Glu	Leu	Ser	Leu	Ala	Asn	Cys	Ser	Thr	Thr	Ala	Arg
			580					585					590		
Thr	Gln	Arg	Trp	Gln	Leu	Asp	Thr	Gly	Ala	Gly	Ala	Leu	Thr	Leu	Arg
		595					600					605			
Asn	Ala	Ile	Ser	Gln	Leu	His	Leu	Thr	Glu	Arg	Ala	Ser	Asp	Gly	Ala
	610					615					620				
Ala	Val	Gln	Thr	Thr	Gly	Ala	Thr	Arg	Leu	Thr	Ala	Arg	Ala	Ala	
625					630						635				

---

What is claimed is:

1. An isolated bacterium, comprising:  
*Lactococcus lactis* PrtP (SEQ ID NO: 2); and  
 at least one protease selected from the group consisting of  
*Lactococcus lactis* HtrA (SEQ ID NO: 1), *Lactococcus*  
*lactis* PrtM (SEQ ID NO: 3), *Lactococcus lactis* CluA  
 (SEQ ID NO: 4), *Streptococcus gordonii* SspA (SEQ ID  
 NO: 5), *Streptococcus mutans* Pac (SEQ ID NO: 6),

60

*Lactococcus lactis* InbA (SEQ ID NO: 7), *Lactobacillus*  
*johnsonii* HtrH-like proteinase (SEQ ID NO: 8), *Lacto-*  
*bacillus acidophilus* HtrH-like proteinase (SEQ ID NO:  
 9), and *Streptococcus thermophilus* exported proteinase  
 (SEQ ID NO: 10),

65 wherein the isolated bacterium is engineered to overexpress  
*Lactococcus lactis* PrtP (SEQ ID NO: 2) and the at least one  
 protease selected from the group consisting of *Lactococcus*

*lactis* HtrA (SEQ ID NO: 1), *Lactococcus lactis* PrtM (SEQ ID NO: 3), *Lactococcus lactis* CluA (SEQ ID NO: 4), *Streptococcus gordonii* SspA (SEQ ID NO: 5), *Streptococcus mutans* Pac (SEQ ID NO: 6), *Lactococcus lactis* InbA (SEQ ID NO: 7), *Lactobacillus johnsonii* HtrH-like proteinase (SEQ ID NO: 8), *Lactobacillus acidophilus* HtrH-like proteinase (SEQ ID NO: 9), and *Streptococcus thermophilus* exported proteinase (SEQ ID NO: 10), and wherein the isolated bacterium promotes the inhibition or removal of a biofilm.

2. The isolated bacterium as claimed in claim 1 wherein the bacterium comprises *Lactococcus lactis* PrtP (SEQ ID NO: 2) and *Lactococcus lactis* HtrA (SEQ ID NO: 1).

3. The isolated bacterium as claimed in claim 1 wherein the bacterium comprises *Lactococcus lactis* PrtP (SEQ ID NO: 2) and *Lactococcus lactis* PrtM (SEQ ID NO: 3).

4. The isolated bacterium as claimed in claim 1 wherein the bacterium comprises *Lactococcus lactis* PrtP (SEQ ID NO: 2) and *Lactococcus lactis* CluA (SEQ ID NO: 4).

5. The isolated bacterium as claimed in claim 1 wherein the bacterium comprises *Lactococcus lactis* PrtP (SEQ ID NO: 2) and *Streptococcus gordonii* SspA (SEQ ID NO: 5).

6. The isolated bacterium as claimed in claim 1 wherein the bacterium comprises *Lactococcus lactis* PrtP (SEQ ID NO: 2) and *Streptococcus mutans* Pac (SEQ ID NO: 6).

7. The isolated bacterium as claimed in claim 1 wherein the bacterium comprises *Lactococcus lactis* PrtP (SEQ ID NO: 2) and *Lactococcus lactis* InbA (SEQ ID NO: 7).

8. The isolated bacterium as claimed in claim 1 wherein the bacterium comprises *Lactococcus lactis* PrtP (SEQ ID NO: 2) and *Lactobacillus johnsonii* HtrH-like proteinase (SEQ ID NO: 8).

9. The isolated bacterium as claimed in claim 1 wherein the bacterium comprises *Lactococcus lactis* PrtP (SEQ ID NO: 2) and *Lactobacillus acidophilus* HtrH-like proteinase (SEQ ID NO: 9).

10. The isolated bacterium as claimed in claim 1 wherein the bacterium comprises *Lactococcus lactis* PrtP (SEQ ID NO: 2) and *Streptococcus thermophilus* exported proteinase (SEQ ID NO: 10).

11. A composition, comprising:  
an isolated bacterium comprising:

*Lactococcus lactis* PrtP (SEQ ID NO: 2); and  
at least one protease selected from the group consisting of *Lactococcus lactis* HtrA (SEQ ID NO: 1), *Lactococcus lactis* PrtM (SEQ ID NO: 3), *Lactococcus lactis* CluA (SEQ ID NO: 4), *Streptococcus gordonii* SspA (SEQ ID NO: 5), *Streptococcus mutans* Pac (SEQ ID NO: 6), *Lactococcus lactis* InbA (SEQ ID NO: 7), *Lactobacillus johnsonii* HtrH-like proteinase (SEQ ID NO: 8), *Lactobacillus acidophilus* HtrH-like proteinase (SEQ ID NO: 9), and *Streptococcus thermophilus* exported proteinase (SEQ ID NO: 10)

wherein the isolated bacterium is engineered to overexpress *Lactococcus lactis* PrtP (SEQ ID NO: 2) and the at least one protease selected from the group consisting of *Lactococcus lactis* HtrA (SEQ ID NO: 1), *Lactococcus lactis* PrtM (SEQ ID NO: 3), *Lactococcus lactis* CluA (SEQ ID NO: 4), *Streptococcus gordonii* SspA (SEQ ID NO: 5), *Streptococcus mutans* Pac (SEQ ID NO: 6), *Lactococcus lactis* InbA (SEQ ID NO: 7), *Lactobacillus johnsonii* HtrH-like proteinase (SEQ ID NO: 8), *Lactobacillus acidophilus* HtrH-like proteinase (SEQ ID NO: 9), and *Streptococcus thermophilus* exported proteinase (SEQ ID NO: 10),

wherein the composition at least partially inhibits or at least partially removes a biofilm.

12. The composition as claimed in claim 11 wherein the composition comprises:

an isolated bacterium comprising:

*Lactococcus lactis* PrtP (SEQ ID NO: 2) and *Lactococcus lactis* HtrA (SEQ ID NO: 1).

13. The composition as claimed in claim 11 wherein the composition comprises:

an isolated bacterium comprising:

*Lactococcus lactis* PrtP (SEQ ID NO: 2) and *Lactococcus lactis* CluA (SEQ ID NO: 4).

14. The composition as claimed in claim 11 wherein the composition is in the form of a gum.

15. The composition as claimed in claim 11 wherein the composition is in the form of a cheesy tooth mask.

16. The composition as claimed in claim 11 wherein the composition further comprises at least one of more of cleaning agents, flavorants, colorants, preservatives, stabilizers, perfumes, antimicrobials, and therapeutic agents.

17. The composition as claimed in claim 11 wherein the composition is contained in an abiotic matrix.

18. The composition as claimed in claim 11 wherein the composition is ingestible.

19. The composition as claimed in claim 11 further comprising at least one antibody selected from the group consisting of *Lactococcus lactis* HtrA antibody, *Lactococcus lactis* PrtP antibody, *Lactococcus lactis* PrtM antibody, *Lactococcus lactis* CluA antibody, *Streptococcus gordonii* SspA antibody, *Streptococcus mutans* Pac antibody, *Lactococcus lactis* InbA antibody, *Lactobacillus johnsonii* HtrH-like proteinase antibody, *Lactobacillus acidophilus* HtrH-like proteinase antibody, and *Streptococcus thermophilus* exported proteinase antibody.

20. A method for removing a biofilm, comprising contacting a biofilm or a biofilm surface with a composition according to claim 11, wherein biofilm formation is reduced or the biofilm is at least partially removed.

21. The method as claimed in claim 20 wherein the composition further comprises at least one antibody selected from the group consisting of *Lactococcus lactis* HtrA antibody, *Lactococcus lactis* PrtP antibody, *Lactococcus lactis* PrtM antibody, *Lactococcus lactis* CluA antibody, *Streptococcus gordonii* SspA antibody, *Streptococcus mutans* Pac antibody, *Lactococcus lactis* InbA antibody, *Lactobacillus johnsonii* HtrH-like proteinase antibody, *Lactobacillus acidophilus* HtrH-like proteinase antibody, and *Streptococcus thermophilus* exported proteinase antibody.

22. The method as claimed in claim 20 wherein the step of contacting comprises contacting at least one of a biotic surface or biofilm on a biotic surface.

23. The method as claimed in claim 22 wherein the biotic surface comprises an oral surface.

24. The method as claimed in claim 20 wherein the step of contacting comprising contacting at least one of an abiotic surface or a biofilm formed on an abiotic surface.

25. The method as claimed in claim 20 wherein the step of contacting comprises contacting the biofilm for a period of time such that the biofilm is at least partially removed.

26. The method as claimed in claim 20 wherein the step of contacting comprises contacting the biofilm surface for a period of time such that biofilm formation on the biofilm surface is reduced.

27. The composition as claimed in claim 11 wherein the composition comprises:

an isolated bacterium comprising:

*Lactococcus lactis* PrtP (SEQ ID NO: 2) and *Lactococcus lactis* PrtM (SEQ ID NO: 3).

## 159

28. The composition as claimed in claim 11 wherein the composition comprises:

an isolated bacterium comprising:

*Lactococcus lactis* PrtP (SEQ ID NO: 2) and *Streptococcus gordonii* SspA (SEQ ID NO: 5).

29. The composition as claimed in claim 11 wherein the composition comprises:

an isolated bacterium comprising:

*Lactococcus lactis* PrtP (SEQ ID NO: 2) and *Streptococcus mutans* Pac (SEQ ID NO: 6).

30. The composition as claimed in claim 11 wherein the composition comprises:

an isolated bacterium comprising:

*Lactococcus lactis* PrtP (SEQ ID NO: 2) and *Lactococcus lactis* InbA (SEQ ID NO: 7).

31. The composition as claimed in claim 11 wherein the composition comprises:

an isolated bacterium comprising:

*Lactococcus lactis* PrtP (SEQ ID NO: 2) and *Lactobacillus johnsonii* HtrH-like proteinase (SEQ ID NO: 8).

32. The composition as claimed in claim 11 wherein the composition comprises:

an isolated bacterium comprising:

*Lactococcus lactis* PrtP (SEQ ID NO: 2) and *Lactobacillus acidophilus* HtrH-like proteinase (SEQ ID NO: 9).

33. The composition as claimed in claim 11 wherein the composition comprises:

## 160

an isolated bacterium comprising:

*Lactococcus lactis* PrtP (SEQ ID NO: 2) and *Streptococcus thermophilus* exported proteinase (SEQ ID NO: 10).

34. The composition as claimed in claim 11 further comprising at least one antibody selected from the group consisting of *Lactococcus lactis* HtrA receptor antibody, *Lactococcus lactis* PrtP receptor antibody, *Lactococcus lactis* PrtM receptor antibody, *Lactococcus lactis* CluA receptor antibody, *Streptococcus gordonii* SspA receptor antibody, *Streptococcus mutans* Pac receptor antibody, *Lactococcus lactis* InbA receptor antibody, *Lactobacillus johnsonii* HtrH-like proteinase receptor antibody, *Lactobacillus acidophilus* HtrH-like proteinase receptor antibody, and *Streptococcus thermophilus* exported proteinase receptor antibody.

35. The method as claimed in claim 20 wherein the composition further comprises at least one antibody selected from the group consisting of *Lactococcus lactis* HtrA receptor antibody, *Lactococcus lactis* PrtP receptor antibody, *Lactococcus lactis* PrtM receptor antibody, *Lactococcus lactis* CluA receptor antibody, *Streptococcus gordonii* SspA receptor antibody, *Streptococcus mutans* Pac receptor antibody, *Lactococcus lactis* InbA receptor antibody, *Lactobacillus johnsonii* HtrH-like proteinase receptor antibody, *Lactobacillus acidophilus* HtrH-like proteinase receptor antibody, and *Streptococcus thermophilus* exported proteinase receptor antibody.

\* \* \* \* \*